preferred em invention inc for inhibiting growth. A embodiment includes a m stimulating e proliferation. highly prefer of the invent method for in endothelial c A highly preferred em includes a m stimulating growth. An a preferred em invention inc for inhibiting growth. Embodiment includes a m stimulating a endothelial c alternative h embodiment includes a m stimulating a endothelial c alternative h embodiment includes a m include	a method a method othelial cell ly preferred invention for	lternative mbodiment cludes a ing oliferation. I	indothelial cell alternative highly bodiment of the cludes a method gendothelial cell A highly preferred of the invention ethod for	An preferred e invention for creasing) helial cells.
. 4	preferred embodir invention includes for inhibiting end growth. A high embodiment of th includes a method	proliferation. An a highly preferred e of the invention ir method for inhibit endothelial cell pr A highly preferred embodiment of th includes a method	stimulating endott growth. An altern preferred embodir invention includes for inhibiting end growth. A hig embodiment of th includes a method stimulating apopted.	endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells.
	C		Cardiovasc Res 45(3): 788-794 (2000); Messmer et al., Br J Pharmacol 127(7): 1633-1640 (1999); and J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety.	used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine

embodiment of the invention includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial
(bAEC), which are an example of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.					-																		
																								-					
											-																		

	•				all &	angioniatosis,	
					hem	hemangioendothelioma,	
					ang	angiosarcoma,	
					haeı	haemangiopericytoma,	
					lym	lymphangioma,	
					lym	lymphangiosarcoma. Highly	<u> </u>
			_		pref	preferred indications also	
	_				incl	include cancers such as,	
					pros	prostate, breast, lung, colon,	
					pan	pancreatic, esophageal,	
					ston	stomach, brain, liver, and	
					urin	urinary cancer. Preferred	
					ipui	indications include benign	
					dys	dysproliferative disorders and	<u>۔</u> و
			-7		pre-	pre-neoplastic conditions, such	ch
					as, i	as, for example, hyperplasia,	
		-			met	metaplasia, and/or dysplasia.	•
·			**,		Hig	Highly preferred indications	
					also	also include arterial disease,	
					snc	such as, atherosclerosis,	
					hyp	hypertension, coronary artery	Z
					dise	disease, inflammatory	
	•			_	vasc	vasculitides, Reynaud"s	
					dise	disease and Reynaud"s	
					bhe	phenomenom, aneurysms,	
					rest	restenosis; venous and	
					lym	lymphatic disorders such as	
					thro	thrombophlebitis,	
					lym	lymphangitis, and	
					lym	lymphedema; and other	
			-				_

peripheral vascular disease,	dica	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred
																										_			

indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	are invention include using polypeptides of the invention odified (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, of the Vascular Disease, CAM-1 Atherosclerosis, Restenosis,
		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1
		Production of ICAM-1
		HMDAQ29 1278
		330

Stroke, and Asthma.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an
expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
	1278
	НМБАQ29
	330

infectious disease as described below under "Infectious Disease"). Preferred	autoimmune diseases (e.g.,	Inpus erythematosis, multiple	sclerosis and/or as described	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin's disease),	melanoma, and prostate,
(including antibodies and agonists or antagonists of the invention) to increase cAMP	and regulate CKEB transcription factors, and	modulate expression of genes involved in a wide variety of	cell functions. Exemplary	through the cAMP response	element that may be used or	routinely modified to test	cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are
											- 49														

breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis,	AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,	hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy. A preferred embodiment of	the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative
publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.			Assays for the activation of	transcription through the Serum Response Element (SRE) are well-known in the art and may be used or
			Activation of	transcription through serum response element in immune cells (such
			1279	
			HMFA148	
				331

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preferred embodiment of the invention includes a method for etimulating (e.g.	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications
routinely modified to assess the ability of polypeptides of	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	withing in proping land
as T-cells).									-																			
			_						-																			
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				through the ATCC). Exemplary mouse T cells that	include neoplastic diseases (e.g., leukemia, lymphoma,
				may be used according to these assays include the CTLL cell	and/or as described below under "Hyperproliferative
**	. =			line, which is an IL-2	Disorders"). Additionally,
	_			dependent suspension culture	highly preferred indications
		d.2277		of T cells with cytotoxic	include neoplasms and
				activity.	cancers, such as, for example,
			_		leukemia, lymphoma,
-					melanoma, glioma (e.g.,
					malignant glioma), solid
					tumors, and prostate, breast,
					lung, colon, pancreatic,
-					esophageal, stomach, brain,
					liver and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
		-			conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
-					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
	,				myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humor
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1279
	HMEA148
	331

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cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells
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								•									• • • • • • • • • • • • • • • • • • • •						***							
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	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders. An additional highly preferred
(HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
	1280
	HMECK83
	332

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infectious disease as described below under "Infectious Disease")	inc	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,
agonists or antagonists of the invention) include assays	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.		
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	-								-															-				

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	d A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.,
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of
	Production of IL-6
	1281
	HMEET96
	333

	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
 	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
 	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
 	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,

				which are herein incorporated by reference in its entirety.	pancreatic, esophageal, stomach, brain, liver and
_				be used according to these	unnary cancer. Ourer presence indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or otherwise known in the art.	pre-neoplastic conditions, such as, for example, hyperplasia.
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HMEET96	1281	Inhibition of	Reporter Assay: construct	

	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and
ng its its al., the	Endothelial cells, which are cells that line blood vessels, and are involved in functions at that include, but are not limited at to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells in that may be used in ICAM in production assays include ne human umbilical vein ca
ion.	Production of ICAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1281
	HMEET96
	333

cardiovascular disorders (such as described below under "Immune Activity", "Blood-	Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred	and cancers such as, for example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benien dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.		
endothelial cells (HUVEC), and are available from commercial sources. The	expression of ICAM (CD54),a intergral membrane protein, can be upregulated by cytokines or other factors, and	in mediating immune and endothelial cell interactions leading to immune and inflammatory responses.	expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1	expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al.,	Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell

334	HMIAL37	1282	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Kinase assay. JNK kinase assays for signal transduction, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., and other as the contract of the contrac
	angi.			Cell Res 247(2): 495-504	described below under
				(1999); Kyriakis JM, Biochem	"Hyperproliferative

Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.	1																								
Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and
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terminal kin mitogen-ac kinase in hamitogen-ac and activation of IL-10 HMIAL37 1282 Production of IL-10 Assays for and activation of T- and activation well known well known well known well known well activated and activation of Il-10 well known well known well activated and activation well known well activated and activated well activated activated we					activation of c-Jun NH2-	notes y
HMIAL37 1282 Production of IL-10 and activation of Troells.					terminal kinase and p38	
HMIAL37 1282 Production of IL-10 and activation of Treath.					mitogen-activated protein	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					kinase in human eosinophils"	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Clin Exp Immunol;	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Oct;122(1):20-7 (2000);	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Hebestreit H, et al.,	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					"Disruption of fas receptor	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					signaling by nitric oxide in	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					eosinophils" J Exp Med; Feb	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					2;187(3):415-25 (1998); J	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Allergy Clin Immunol 1999	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Sep;104(3 Pt 1):565-74; and,	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Sousa AR, et al., "In vivo	
HMIAL37 1282 Production of IL-10 and activation of Teals.					resistance to corticosteroids in	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					bronchial asthma is associated	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					with enhanced	
HMIAL37 1282 Production of IL-10 and activation of Teals.					phosyphorylation of JUN N-	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					terminal kinase and failure of	
HMIAL37 1282 Production of IL-10 and activation of Teals.					prednisolone to inhibit JUN N-	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					terminal kinase	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					phosphorylation" J Allergy	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					Clin Immunol; Sep;104(3 Pt	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					1):565-74 (1999); the contents	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					of each of which are herein	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					incorporated by reference in its	
HMIAL37 1282 Production of IL-10 and activation of T-cells.					entirety.	and the second s
and activation of T-cells.		HMIAL37	1282	Production of IL-10	Assays for production of IL-10	Highly preferred indications
	334		-	and activation of 1-	and activation of 1-cells are	include allergy and asthma.
				cells.	well known in the art and may	Additional highly preferred
l pe used or					be used or routinely modified	indications include immune

der der T T T T	
and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.	
to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety.	used according to these assays
to as polyl (incl.) (incl.) (incl.) agon invertible inhibit and (incl.) Exer used asses asses polyl the invertible in	nseq
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	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, induce
	Production of MCP-1
	1283
	HMIAP86
	335

chemotaxis, and modulate	Additional highly preferred
immune cell activation.	indications include
Exemplary assays that test for	inflammation and
immunomodulatory proteins	inflammatory disorders.
evaluate the production of cell	Preferred indications include
surface markers, such as	blood disorders (e.g., as
monocyte chemoattractant	described below under
protein (MCP), and the	"Immune Activity", "Blood-
activation of monocytes and T	Related Disorders", and/or
cells. Such assays that may be	"Cardiovascular Disorders").
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted

				be used according to these	organs and tissues,
				assays may be isolated using	hemophilia, hypercoagulation,
				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
			-	and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HMIAP86	1283	Production of	MIP-1alpha FMAT. Assays	A highly preferred
335			MIP1alpha	for immunomodulatory	embodiment of the invention
			•	proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
				known in the art and may be	includes a method for
			The second secon		

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inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is	infection (e.g., an infectious disease as described below	under "Infectious Disease"). Preferred indications include	blood disorders (e.g., as	described below under	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous
used or routinely modified to assess the ability of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) to mediate	chemotaxis, and modulate T	cell differentiation. Exemplary	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and
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al., Transp Immunol 8(1):17- 29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. by dendritic immunomodulatory proteins					Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
1997); Verhasselt et al., J.					al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
Immunol 138:2919-2925 (1997); and Nardelli et al., J. Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and the produced by activated by activated by activated and alpha by dendritic immunomodulatory proteins and allong the produced by activated by act					29 (2000); Verhasselt et al., J	suppression of immune
(1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for immunomodulatory proteins					Immunol 158:2919-2925	reactions to transplanted
Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins produced by activated by activate					(1997); and Nardelli et al., J	organs and tissues, hemophilia,
(1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins mandlunged by activated immunomodulatory proteins and immunomodulat					Leukoc Biol 65:822-828	hypercoagulation, diabetes
which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins mandless and the properties of the properties of the properties of the production of TNF immunomodulatory proteins and the properties of the properties of the properties of the properties of the production of TNF immunomodulatory proteins and the properties of the					(1999), the contents of each of	mellitus, endocarditis,
hy reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins					which are herein incorporated	meningitis, Lyme Disease,
Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and the production of the production o					by reference in its entirety.	asthma, and allergy.
be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and the production of TNF immunomodulatory proteins and the production of					Human dendritic cells that may	Preferred indications also
assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for immunomodulatory proteins					be used according to these	include neoplastic diseases
techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and produced by activated the activated that are incompared to the activated the activated that activated the activated th					assays may be isolated using	(e.g., leukemia, lymphoma,
Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and produced by activated by activ					techniques disclosed herein or	and/or as described below
Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and the activated by					otherwise known in the art.	under "Hyperproliferative
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and immunomodulatory proteins and immunomodulatory proteins are alpha by dendritic immunomodulatory proteins					Human dendritic cells are	Disorders"). Highly preferred
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and immunomodulatory proteins and immunomodulatory proteins and immunomodulatory proteins and immunomodulatory proteins immunomo					antigen presenting cells in	indications include neoplasms
when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins and produced by activated by activated					suspension culture, which,	and cancers, such as, leukemia,
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins					when activated by antigen	lymphoma, prostate, breast,
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins					and/or cytokines, initiate and	lung, colon, pancreatic,
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins					upregulate T cell proliferation	esophageal, stomach, brain,
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins					and functional activities.	liver, and urinary cancer. Other
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins						preferred indications include
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins						benign dysproliferative
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins						disorders and pre-neoplastic
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins						conditions, such as, for
HMIAP86 1283 Production of TNF TNFa FMAT. Assays for alpha by dendritic immunomodulatory proteins						example, hyperplasia,
HMIAP86 1283 Production of TNF a FMAT. Assays for alpha by dendritic immunomodulatory proteins				-		metaplasia, and/or dysplasia.
alpha by dendritic immunomodulatory proteins		HMIAP86	1283	Production of TNF	TNFa FMAT. Assays for	A highly preferred
neodine d by activated	335			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
produced by activated				cells	produced by activated	includes a method for

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inhibiting (e.g., decreasing)	INF alpha production. An	alternative highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly
macrophages, T cells,	libroblasts, smooth muscie,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J
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											- 	·																		

disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as
	Assay that measures the production of the chemokine interleukin-8 (IL-8) from immune cells (such as the EOL-1 human eosinophil cell line) are well known in the art (for example, measurement of IL-8 production by FMAT) and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit. Eosinophils are a type of immune cell important in allergic responses: they are
	Production of IL-8 by immune cells (such as the human EOL-1 eosinophil cells)
	1283
	HMIAP86
	335

			recruited to tissues and mediate the inflammtory response of late stage allergic reaction. IL8 is a strong immunomodulator and may have a potential proinflammatory role in immunological diseases and	described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under
HMIAP86	1283	IL-10 in Human T- cell 2B9	asthma).	Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.
HMIAP86	1283	Production of IL-8 by by endothelial cells (such as Human Umbilical Cord Endothelial Cells).	Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8. For example, FMAT may be used or routinely modified to assess the ability of polypeptides of the invention (including	Highly preferred indications include immunological and inflammatory disorders (e.g., such as allergy, asthma, leukemia, etc. and as described below under "Immune Activity", and "Blood-Related Disorders"). Highly preferred indications also includie autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below),

				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
				vascular permeability, vascular	consequent complications
				tone, and immune cell	(such as acute respiratory
				extravasation. Endothelial	distress syndrome and
				cells play a pivotal role in the	systemic ischemia-reperfusion
				initiation and perpetuation of	resulting from septic shock),
				inflammation and secretion of	restnosis and atherosclerosis.
				IL-8 may play an important	
				role in recruitment and	
				activation of immune cells	
				such as neutrophils,	
				macrophages, and lymphocytes	
	HMIAP86	1283	Production of	Assays for measuring	Highly preferred indications
335			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
		i	(HUVEC))	(including antibodies and	inflammation and

			_																										
inflammatory disorders, immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.						
agonists or antagonists of the invention) to regulate VCAM	expression. For example,	FMAT may be used to meaure	the upregulation of cell surface	VCAM-1 expresssion in	endothelial cells. Endothelial	cells are cells that line blood	vessels, and are involved in	functions that include, but are	not limited to, angiogenesis,	vascular permeability, vascular	tone, and immune cell	extravasation. Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are available from	commercial sources. The	expression of VCAM	(CD106), a membrane-	associated protein, can be	upregulated by cytokines or	other factors, and contributes	to the extravasation of	lymphocytes, leucocytes and	other immune cells from blood	vessels; thus VCAM	expression plays a role in	7 20 0 22 22 22 22 22 22 22 22 22 22 22 2
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				inflammatory responses.	
	HMKCG09	1284	Regulation of	Assays for the regulation (i.e.	Highly preferred indications
336			viability or	increases or decreases) of	include eosinophilia, asthma,
		44	proliferation of	viability and proliferation of	allergy, hypersensitivity
			immune cells (such	cells in vitro are well-known in	reactions, inflammation, and
			as human	the art and may be used or	inflammatory disorders.
			eosinophil EOL-1	routinely modified to assess	Additional highly preferred
			cells).	the ability of polypeptides of	indications include immune
				the invention (including	and hematopoietic disorders
			-	antibodies and agonists or	(e.g., as described below under
				antagonists of the invention) to	"Immune Activity", and
				regulate viability and	"Blood-Related Disorders"),
				proliferation of eosinophil cells	autoimmune diseases (e.g.,
				and cell lines. For example,	rheumatoid arthritis, systemic
				the CellTiter-Gloô	lupus erythematosis, Crohn"s
				Luminescent Cell Viability	disease, multiple sclerosis
				Assay (Promega Corp.,	and/or as described below),
				Madison, WI, USA) can be	immunodeficiencies (e.g., as
				used to measure the number of	described below). Highly
				viable cells in culture based on	preferred indications also
				quantitation of the ATP	include boosting or inhibiting
				present which signals the	immune cell proliferation.
				presence of metabolically	Preferred indications include
				active cells. Eosinophils are a	neoplastic diseases (e.g.,
				type of immune cell important	leukemia, lymphoma, and/or as
				in allergic responses; they are	described below under
				recruited to tissues and	"Hyperproliferative
				mediate the inflammtory	Disorders"). Highly preferred
				response of late stage allergic	indications include boosting an
				reaction. Eosinophil cell lines	eosinophil-mediated immune
				that may be used according to	response, and suppressing an

				these assays are publicly available and/or may be routinely generated. Exemplary eosinophil cells that may be used according to these assays include EOL-1 Cells.	eosinophil-mediated immune response.
336	HMKCG09	1284	Production of IFNgamma using a	IFNgamma FMAT. IFNg plays a central role in the immune	A highly preferred embodiment of the invention
apa sijes dan d				a proinflammatory cytokine. IFNg promotes TH1 and	stimulating the production of IFNg. An alternative highly
		·		inhibits TH2 differentiation; promotes IgG2a and inhibits	preferred embodiment of the invention includes a method
				IgE secretion; induces macrophage activation; and	for inhibiting the production of IFNg. Highly preferred
				increases MHC expression.	SI
				Assays for immunomodulatory proteins produced by T cells	disorders (e.g., as described below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
				activities and inhibit TH2	"Cardiovascular Disorders"),
				helper cell functions are well	and infection (e.g., viral
				known in the art and may be used or routinely modified to	infections, tuberculosis, infections associated with
				assess the ability of	chronic granulomatosus
				polypeptides of the invention	disease and malignant
				(including antibodies and	osteoporosis, and/or as
_				agonists or antagonists of the	described below under
				invention) to mediate	"Infectious Disease"). Highly
				immunomodulation, regulate	preferred indications include

inflammato	inflammatory activities,	autoimmune disease (e.g.,
modulate T	=	rheumatoid arthritis, systemic
function, an		lupus erythematosis, multiple
humoral or		sclerosis and/or as described
 immunity.	says	below), immunodeficiency
that test for		(e.g., as described below),
immunomo	immunomodulatory proteins	boosting a T cell-mediated
evaluate the	evaluate the production of	immune response, and
cytokines, s	cytokines, such as Interferon	suppressing a T cell-mediated
gamma (IF)	gamma (IFNg), and the	immune response. Additional
activation o	ıch	highly preferred indications
assays that	assays that may be used or	include inflammation and
 routinely m		inflammatory disorders.
omoundi	ity of	Additional preferred
polypeptide		indications include idiopathic
(including a	(including antibodies and	pulmonary fibrosis. Highly
agonists or	the	preferred indications include
 invention) i		neoplastic diseases (e.g.,
disclosed in	disclosed in Miraglia et al., J	leukemia, lymphoma,
Biomolecul	Biomolecular Screening 4:193-	melanoma, and/or as described
204 (1999);	204 (1999); Rowland et al.,	below under
"Lymphocy	"Lymphocytes: a practical	"Hyperproliferative
approach" (091	Disorders"). Highly preferred
(2000); Go	(2000); Gonzalez et al., J Clin	indications include neoplasms
Lab Anal 8	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Billiau et al	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
Sci 856:22-	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
et al., Annu	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:749-795	15:749-795 (1997), and	esophageal, stomach, brain,
 Rheumatol	Rheumatology (Oxford)	liver and urinary cancer. Other
38(3):214-2	38(3):214-20 (1999), the	preferred indications include

				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
		•		responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMKCG09	1284	Production of IL-10	Assays for production of IL-10	Highly preferred indications
336			and activation of T-	and activation of T-cells are	include allergy and asthma.
1			cells.	well known in the art and may	Additional highly preferred
				be used or routinely modified	indications include immune
				to assess the ability of	and hematopoietic disorders
				polypeptides of the invention	(e.g., as described below under
				including antibodies and	"Immune Activity", and
				agonists or antagonists of the	"Blood-Related Disorders"),

autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis	immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune	response, and suppressing a T cell-mediated immune response.										
invention) to stimulate or rhinhibit production of IL-10 rh and/or activation of T-cells. Exemplary assays that may be dissed or routinely modified to	————	agonists or antagonists of the invention) to modulate IL-10 coproduction and/or T-cell re	proliferation include, for example, assays such as	Robinson, DS, et al., "Th-2	Cytoxines in ancign disease Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-	helper type 2 cell-directed therapy for asthma"	Pharmacology & Therapeutics; 88: 187-196 (2000); the	contents of each of which are herein incorporated by	reference in their entirety. Exemplary cells that may be	used according to these assays include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of 1h2 cell activation. Th2 cells are

		A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for
a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK
	TNFa in Human T-cell 293T	Activation of Natural Killer Cell ERK Signaling Pathway.
	1285	1285
	HMMAH60	HMMAH60
	337	337

	used or routinely modified to	inhibiting natural killer cell
	activity of polypeptides of the	ıtio
	invention (including antibodies	neoplastic diseases (e.g., as
 	and agonists or antagonists of	described below under
	the invention) include the	"Hyperproliferative
 	assays disclosed in Forrer et	Disorders"), blood disorders
	al., Biol Chem 379(8-9):1101-	(e.g., as described below under
	1110 (1998); Kyriakis JM,	"Immune Activity",
	Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
	(1999); Chang and Karin,	and/or "Blood-Related
	Nature 410(6824):37-40	Disorders"), immune disorders
	(2001); and Cobb MH, Prog	(e.g., as described below under
	Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
-	500 (1999); the contents of	infections (e.g., as described
 	each of which are herein	below under "Infectious
	incorporated by reference in its	Disease"). Preferred
	entirety. Natural killer cells	indications include blood
 -	that may be used according to	disorders (e.g., as described
	these assays are publicly	below under "Immune
	available (e.g., through the	Activity", "Blood-Related
	ATCC). Exemplary natural	Disorders", and/or
 	killer cells that may be used	"Cardiovascular Disorders").
	according to these assays	Highly preferred indications
 	include the human natural	include autoimmune diseases
	killer cell lines (for example,	(e.g., rheumatoid arthritis,
	NK-YT cells which have	systemic lupus erythematosis,
	cytolytic and cytotoxic	multiple sclerosis and/or as
 	activity) or primary NK cells.	described below) and
 		immunodeficiencies (e.g., as
		described below). Additional

				highly preferred indications	d indications
				include inflammation and	nation and
				inflammatory disorders.	lisorders.
				Highly preferred indications	ed indications
				also include cancers such as,	ncers such as,
				kidney, melanoma, prostate,	ma, prostate,
				breast, lung, co	breast, lung, colon, pancreatic,
				esophageal, stomach, brain,	mach, brain,
				liver, urinary cancer,	ancer,
				Iymphoma and leukemias.	leukemias.
				Other preferred indications	l indications
				include benign	include benign dysproliferative
				disorders and pre-neoplastic	re-neoplastic
				conditions, such as, for	h as, for
				example, hyperplasia,	rplasia,
				metaplasia, and/or dysplasia.	I/or dysplasia.
				Other highly preferred	referred
				indications include,	lude,
				pancytopenia, leukopenia,	leukopenia,
				leukemias, Hoo	leukemias, Hodgkin's disease,
				acute lymphocytic anemia	ytic anemia
				(ALL), arthritis, asthma,	s, asthma,
				AIDS, granulo	AIDS, granulomatous disease,
				inflammatory bowel disease,	owel disease,
				sepsis, psoriasis, immune	s, immune
				reactions to transplanted	nsplanted
				organs and tissues,	nes,
				endocarditis, n	endocarditis, meningitis, Lyme
				Disease, and allergies.	lergies.
337	HMMAH60	1285	VEGF in SW480		

n of IL-10 Highly preferred indications		and may Additional highly preferred	modified indications include immune		nvention (e.g., as described below under		its of the "Blood-Related Disorders"),	te or autoimmune diseases (e.g.,	IL-10 rheumatoid arthritis, systemic	F-cells. lupus erythematosis, Crohn"s	at may be disease, multiple sclerosis	diffed to and/or as described below),	immunodeficiencies (e.g., as	ibodies of described below), boosting a T	ing cell-mediated immune	its of the response, and suppressing a T	te IL-10 cell-mediated immune	cell response.	for	1 as	d in:	"Th-2	disease"	956-968	al., "T-	ected	-	erapeutics;	the	hich are
Assays for production of IL-10		well known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate or	inhibit production of IL-10	and/or activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are
Production of IL-10	and activation of T-	cells.				-																								
1285																					-									
HMMAH60	•																													
	337																													

	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is
herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Production of MIP1alpha
	1286
	HMQDF12
	338

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infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	
(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	E
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									-																					

29 (2000); Verhasselt et al., J suppression of immune Inmunol 158:2919-2925 reactions to transplanted	(1997); and Nardelli et al., J organs and tissues, hemophilia, I entoc Biol 65:822-828	٠	eq	-	Human dendritic cells that may Freiefred indications also he used according to these	gu	techniques disclosed herein or and/or as described below	otherwise known in the art. under "Hyperproliferative	Human dendritic cells are Disorders"). Highly preferred	antigen presenting cells in indications include neoplasms	suspension culture, which, and cancers, such as, leukemia,	when activated by antigen lymphoma, prostate, breast,		upregulate T cell proliferation esophageal, stomach, brain,	and functional activities. liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	TNFa FMAT. Assays for A highly preferred	immunomodulatory proteins embodiment of the invention	produced by activated includes a method for	macrophages, T cells, inhibiting (e.g., decreasing)	fibroblasts, smooth muscle, TNF alpha production. An	rt a
29 (2000); V Immunol 15	(1997); and I enkoc Biol	(1999), the	which are he	by reference	Human den	assays may	techniques	otherwise k	Human den	antigen pres	suspension	when activa	and/or cytol	upregulate	and function							Production of TNF TNFa FMA		_		fibroblasts,	and other co
														-			-					F12 1286					
					****				-													HMODF12	338)			

wide variety of inflammatory
and cytotoxic effects on a
variety of cells are well known
in the art and may be used or
routinely modified to assess
the ability of polypeptides of
the invention (including
antibodies and agonists or
antagonists of the invention) to
mediate immunomodulation,
modulate inflammation and
cytotoxicity. Exemplary
assays that test for
immunomodulatory proteins
evaluate the production of
cytokines such as tumor
necrosis factor alpha (TNFa),
and the induction or inhibition
of an inflammatory or
cytotoxic response. Such
assays that may be used or
routinely modified to test
immunomodulatory activity of
polypeptides of the invention
(including antibodies and
agonists or antagonists of the
invention) include assays
disclosed in Miraglia et al., J
Biomolecular Screening 4:193-
204(1999); Rowland et al.,
"Lymphocytes: a practical

(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, leukemia,	lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung colon, pancreatic.	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL),	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis, suppression of immune
approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J	Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925	(1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incornorated	by reference in its entirety. Human dendritic cells that may	be used according to these assays may be isolated using	techniques disclosed herein or otherwise known in the art.	Human dendritic cells are antigen presenting cells in	suspension culture, which, when activated by antigen	and/or cytokines, initiate and upregulate T cell proliferation	and functional activities.				
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reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
	1286
	HMQDF12
	338

				entirety.	
338	HMQDF12	1286	Caspase (+paclitaxel) in SW480		
339	HMSBX80	1287	CD71 in Human T cells		
	HMSFS21	1288	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
340				by T cells and has strong	embodiment of the invention
			-	effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
		,		IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
		•		hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple

sclerosis and/or as described	below) and	imminodeficiencies (e a as	described below) Highly	ucscriped octow). Ingility	include boosting a R cell-	mediated immine response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach. brain, liver and
agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.
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				Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
340	HMSFS21	1288	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may	Preferred embodiments of the invention include using polypeptides of the invention

			to assess the ability of	of althouses, agoinsts, or antagonists thereoff in
			polypeptides of the invention	detection, diagnosis,
			(including antibodies and	prevention, and/or treatment of
_			agonists or antagonists of the	Inflammation, Vascular
			invention) to regulate ICAM-1	Disease, Athereosclerosis,
			expression. Exemplary assays	Restenosis, and Stroke
			that may be used or routinely	
			modified to measure ICAM-1	
			expression include assays	
			disclosed in: Takacs P, et al,	
			FASEB J, 15(2):279-281	
			(2001); and, Miyamoto K, et	
-			al., Am J Pathol, 156(5):1733-	
			1739 (2000), the contents of	
			each of which is herein	
			incorporated by reference in its	
			entirety. Cells that may be	
-			used according to these assays	
			are publicly available (e.g.,	
			through the ATCC) and/or	
			may be routinely generated.	
			Exemplary cells that may be	
			used according to these assays	
			include microvascular	
			endothelial cells (MVEC).	
HMSGB14	1289	Activation of	Assays for the activation of	Preferred indications
		transcription	transcription through the AP1	include neoplastic diseases
		through AP1	response element are known in	(e.g., as described below under
		response element in	the art and may be used or	"Hyperproliferative
		immune cells (such	routinely modified to assess	Disorders"), blood disorders

as T-cells).	the ability of polypeptides of	(e.g., as described below under
	the invention (including	"Immune Activity",
	antibodies and agonists or	"Cardiovascular Disorders",
	antagonists of the invention) to	and/or "Blood-Related
	modulate growth and other cell	Disorders"), and infection
	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
 	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,

				according to these assays are	liver, and urinary cancer. Other
-				publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the CTLL cell	example, hyperplasia,
				line, which is an IL-2	metaplasia, and/or dysplasia.
		,		dependent suspension-culture	Preferred indications include
				cell line with cytotoxic	arthritis, asthma, AIDS,
,				activity.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
-					myeloma, Burkitt's lymphoma,
					granulomatous disease,
-					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HMSGT42	1290	Activation of	Kinase assay. JNK and p38	A highly preferred
342			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred

	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
 	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	 Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
-	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
1	Exemplary endothelial cells	embodiment of the invention

				_		
includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for	inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac	hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac	hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive	heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular	dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic
that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line	venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular	permeability, vascular tone, and immune cell extravasation.				

hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease.
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																								`						

and cancer. Highly preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include

blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory disorders (e.g.,	inflammatory bowel disease and Crohn's disease), and pain management. Preferred indications include blood disorders (e.g., as described below under ay "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred
	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
	1291
	HMSHM14
2062	343

	and regulate CREB	indications include
	transcription factors, and	autoimmune diseases (e.g.,
	modulate expression of genes	rheumatoid arthritis, systemic
	involved in a wide variety of	lupus erythematosis, multiple
	cell functions. Exemplary	sclerosis and/or as described
	assays for transcription	below), immunodeficiencies
-	through the cAMP response	(e.g., as described below),
	element that may be used or	boosting a T cell-mediated
	routinely modified to test	immune response, and
	cAMP-response element	suppressing a T cell-mediated
_	activity of polypeptides of the	immune response. Additional
	invention (including antibodies	preferred indications include
	and agonists or antagonists of	inflammation and
	the invention) include assays	inflammatory disorders.
	disclosed in Berger et al., Gene	Highly preferred indications
	66:1-10 (1998); Cullen and	include neoplastic diseases
	Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
	216:362-368 (1992); Henthorn	and/or as described below
	et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Genes 15(2):105-117	indications include neoplasms
	(1997); and Belkowski et al., J	and cancers, such as, for
,-	Immunol 161(2):659-665	example, leukemia, lymphoma
-	(1998), the contents of each of	(e.g., T cell lymphoma,
	which are herein incorporated	Burkitt's lymphoma, non-
	by reference in its entirety. T	Hodgkins lymphoma,
	cells that may be used	Hodgkin"s disease),
	according to these assays are	melanoma, and prostate,
	publicly available (e.g.,	breast, lung, colon, pancreatic,
 	through the ATCC).	esophageal, stomach, brain,
	Exemplary mouse T cells that	liver and urinary cancer. Other

				may be used according to these	preferred indications include
				assays include the CTLL cell	benign dysproliferative
_				line, which is a suspension	disorders and pre-neoplastic
				culture of IL-2 dependent	conditions, such as, for
				cytotoxic T cells.	example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
-					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HMSHM14	1291	Activation of	Assays for the activation of	A preferred embodiment of
343			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,

	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate the semm response	Ž
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
-	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below

			assays include the CTLL cell	under "Hyperproliferative
		**	line, which is an IL-2	Disorders"). Additionally.
			dependent suspension culture	highly preferred indications
		· · · · · ·	of T cells with cytotoxic	include neoplasms and
	•		activity.	cancers, such as, for example,
 				leukemia, lymphoma,
 				melanoma, glioma (e.g.,
				malignant glioma), solid
-				tumors, and prostate, breast,
				lung, colon, pancreatic,
				esophageal, stomach, brain,
 -				liver and urinary cancer. Other
				preferred indications include
_				benign dysproliferative
				disorders and pre-neoplastic
	•			conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
_				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
 -				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
_				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
 				disease, neutropenia,
				neutrophilia, psoriasis,
 -				suppression of immune
				reactions to transplanted

					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HMSHM14	1291	Production of	MCP-1 FMAT. Assays for	A highly preferred
343			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
			*	cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for
				modified to assess the ability	inhibiting (e.g., reducing)
				of polypeptides of the	MCP-1 production. A highly
				invention (including antibodies	preferred indication is
				and agonists or antagonists of	infection (e.g., an infectious
				the invention) to mediate	disease as described below
				immunomodulation, induce	under "Infectious Disease").
				chemotaxis, and modulate	Additional highly preferred
				immune cell activation.	indications include
				Exemplary assays that test for	inflammation and
				immunomodulatory proteins	inflammatory disorders.
				evaluate the production of cell	Preferred indications include
	_			surface markers, such as	blood disorders (e.g., as
				monocyte chemoattractant	described below under

protein (MCP), and the	"Immune Activity", "Blood-
 activation of monocytes and T	Related Disorders", and/or
cells. Such assays that may be	"Cardiovascular Disorders").
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
 (including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
 invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
 158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
 herein incorporated by	neutrophilia, psoriasis,
reference in its entirety.	suppression of immune
 Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
 assays may be isolated using	hemophilia, hypercoagulation,
techniques disclosed herein or	diabetes mellitus, endocarditis,
otherwise known in the art.	meningitis (bacterial and
Human dendritic cells are	viral), Lyme Disease, asthma,
antigen presenting cells in	and allergy Preferred
suspension culture, which,	indications also include

				when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
344	HMSHS36	1292	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s

			kinase activity that may be	disease, multiple sclerosis
			used or routinely modified to	and/or as described below).
			test JNK kinase-induced	immunodeficiencies (e.g., as
			activity of polypeptides of the	described below). Highly
			invention (including antibodies	preferred indications also
			and agonists or antagonists of	include boosting or inhibiting
	_		the invention) include the	immune cell proliferation.
			assays disclosed in Forrer et	Preferred indications include
			al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
			1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
			Cell Res 247(2): 495-504	described below under
			(1999); Kyriakis JM, Biochem	"Hyperproliferative
		-	Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
			Chang and Karin, Nature	indications include boosting an
			410(6824):37-40 (2001); and	eosinophil-mediated immune
			Cobb MH, Prog Biophys Mol	response, and suppressing an
-			Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
			the contents of each of which	response.
			are herein incorporated by	
			reference in its entirety.	
			Exemplary cells that may be	
			used according to these assays	
			include eosinophils.	
			Eosinophils are important in	
			the late stage of allergic	
			reactions; they are recruited to	
			tissues and mediate the	
			inflammatory response of late	
			stage allergic reaction.	
			Moreover, exemplary assays	
			that may be used or routinely	

modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nítric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of
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				prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	
	HMSHS36	1292	Activation of	Assays for the activation of	Highly preferred indications
344			transcription through NFAT	transcription through the Nuclear Factor of Activated T	include blood disorders (e.g., as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
	· · · · · · · · · · · · · · · · · · ·		immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
	·			the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
	·			immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
	·····			transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an

infectious disease as described below under "Infectious Disease"). Preferred indications include neonlastic	diseases (e.g., leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders"), Preferred indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal,	stomach, orain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,
infectious classifications (Disease").	diseases (e.g. lymphoma, a below under	"Hyperpi Disorders indication	example, and prost colon, pa	urinary c indication dysprolif	pre-neop as, for ex metaplas Preferred include a	leukopen Hodgkin lymphoc plasmacy myeloma arthritis, disease, i
agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66.1-10 (1998). Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci 11SA	85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al. Int I Biochem Cell	Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and	reseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by	reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.
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				-		

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1292
	HMSHS36
	344

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(e.g., as described below),	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	1 11 m 1 m 1 m 1 m 1 m 1 m 1 m 1 m 1 m
the invention) include assays	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.								
												-								-									

					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
•					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
344	HMSHS36	1292	SEAP in NK 16/STAT6		
	HMSJM65	1293	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
345				by T cells and has strong	embodiment of the invention
				effects on D cells. IL-0	metudes a method for

		participates in IL-4 induced	stimulating (e.g., increasing)
		IgE production and increases	IL-6 production. An alternative
	-	IgA production (IgA plays a	highly preferred embodiment
		role in mucosal immunity).	of the invention includes a
		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
		Deregulated expression of IL-6	reducing) IL-6 production. A
		has been linked to autoimmune	highly preferrred indication is
		disease, plasmacytomas,	the stimulation or enhancement
		myelomas, and chronic	of mucosal immunity. Highly
		hyperproliferative diseases.	preferred indications include
		Assays for immunomodulatory	blood disorders (e.g., as
		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
-		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune

		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders.Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
,		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	,	Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,

and/or cytokines, initiate and lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectious below under "Infectious Disease").	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified be used or routinely modified indications include infection (e.g., an infectious disease as polypeptides of the invention) to regulate NFKB inflammation and transcription factors and as described below under as described below as described
and/o upreg	Activation of Assatranscription transcription transcription transcription transcription well-immune cells (such be us as EOL1 cells). polype (included) inventranscription of the polype inventranscription inventranscription of transcription of
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			- 7.7	gene and binds to the NFKB transcription factor which is	
				upregulated by cytokines and	
				other factors. Exemplary	•
				immune cells that may be used	
				according to these assays	
				include eosinophils such as the	
				human EOL-1 cell line of	
				eosinophils. Eosinophils are a	
				type of immune cell important	
	-			in the allergic responses; they	
				are recruited to tissues and	
				mediate the inflammtory	
				response of late stage allergic	
				reaction. Eol-1 is a human	
				eosinophil cell line.	
	HMSJU68	1294	Glucose Production		
346		-	in H4IIE		
	HMSJU68	1294	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
346			apoptosis of	caspase apoptosis are well	invention include using
			immune cells (such	known in the art and may be	polypeptides of the invention
			as mast cells).	used or routinely modified to	(or antibodies, agonists, or
				assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	asthma, allergy,
				invention) to regulate caspase	hypersensitivity and
				protease-mediated apoptosis in	inflammation.
				immune cells (such as, for	
				example, in mast cells). Mast	
				cells are found in connective	

and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by
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	al a
	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment, skeletal muscle
reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of
	Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway
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	HMSJU68
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cell proliferation is inhibited.	A preferred embodiment of	the invention includes a	method for stimulating muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	stimulated. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	inhibited. Highly preferred	indications include disorders of	the musculoskeletal system.	Preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular
the invention) include assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Nikoulina et al.,	Diabetes 49(2):263-271	(2000); and Schreyer et al.,	Diabetes 48(8):1662-1666	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Rat myoblast cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary rat myoblast cells	that may be used according to	these assays include L6 cells.	L6 is an adherent rat myoblast	cell line, isolated from primary	cultures of rat thigh muscle,	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.							
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Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,
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heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below), neuropathy, vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, infections (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section	below, especially of the urinary tract and skin), carpal	tunnel syndrome and Dupuytren's contracture).	An additional highly preferred indication is obesity and/or	obesity. Additional highly preferred indications include	weight loss or alternatively, weight gain. Additional	highly preferred indications are complications associated with insulin resistance.

Additional highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly	preferred indications include	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,	and liver cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as,	hyperplasia, metaplasia, and/or	uyspiasia.
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346			(+camptothecin) in SW480		
347	HMSKC04	1295	SEAP in 293/ISRE		
347	HMSKC04	1295	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia,

272(49):3 Chang et	272(49):30806-30811 (1997); Chang et al., Mol Cell Biol	lymphoma, and/or as described below under
18(9):498	18(9):4986-4993 (1998); and	"Hyperproliferative
Fraser et a	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
29(3):838	29(3):838-844 (1999), the	indications include neoplasms
contents o	contents of each of which are	and cancers, such as, leukemia,
herein inc	herein incorporated by	lymphoma, prostate, breast,
reference	reference in its entirety. T	lung, colon, pancreatic,
cells that	cells that may be used	esophageal, stomach, brain,
according	according to these assays are	liver, and urinary cancer. Other
publicly a	publicly available (e.g.,	preferred indications include
through th	through the ATCC).	benign dysproliferative
Exemplar	Exemplary mouse T cells that	disorders and pre-neoplastic
may be us	may be used according to these	conditions, such as, for
assays inc	assays include the CTLL cell	example, hyperplasia,
line, whic	line, which is an IL-2	metaplasia, and/or dysplasia.
dependent	dependent suspension-culture	Preferred indications include
cell line w	cell line with cytotoxic	arthritis, asthma, AIDS,
activity.		allergy, anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, psoriasis, suppression
		of immune reactions to
		transplanted organs and
		tissues, endocarditis,
		meningitis, and Lyme Disease.

SEAP in HIB/CRE	Activation of This reporter assay measures Highly preferred indications	activation of the GATA-3	through GATA-3 signaling pathway in HMC-1 rhinitis. Additional preferred	human mast cell line.	immune cells (such Activation of GATA-3 in mast (e.g., an infectious disease as	as mast cells). cells has been linked to described below under	_	production. Assays for the inflammation and		through the GATA3 response Preferred indications also	element are well-known in the include blood disorders (e.g.,	art and may be used or as described below under	routinely modified to assess "Immune Activity", "Blood-	the ability of polypeptides of Related Disorders", and/or		antibodies and agonists or Preferred indications include	antagonists of the invention) to autoimmune diseases (e.g.,	regulate GATA3 transcription rheumatoid arthritis, systemic	factors and modulate lupus erythematosis, multiple		bonse	Zi	assays for transcription described below). Preferred	through the GATA3 response indications include neoplastic	or		GATA3-response element prostate, breast, lung, colon,	activity of polymentides of the pancing acompany
1295 SEAP in HIB/CRE							cytokii	produc	activat	through	elemer	art and	routine	the abi	the inv	antiboc	antago	regulat	factors	express	import	develo	assays	through	elemen	routine	GATA	activity
HMSKC04	HMSKC04							17.8				-															***	
347	177	34/												200						,								

the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell as, for example, hyperplasia, et al., Cold Spring Harb Symp Preferred indications include R5:6342-6346 (1988); Flavell as, for example, hyperplasia, et al., Cold Spring Harb Symp Preferred indications include Rodriguez-Palmero et al., But an incorporated by Immunol 29(12):3914-3924 (1999); Zheng and Flavell, eukemias, Hodgkin's disease, Cells Hat may be used contents of each of which are herein incorporated by inflammatory bowel disease, reference in its entirety. Mast according to these assays are publicly available (e.g., publicly available (e.g., publicly available (e.g., publicly available fe.g., through the ATCC). Exemplary human mast cell ince established from the peripheral blood of a patient with mast	e	e
the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast	the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast	the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Bur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast

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	Highly preferred indications	include allergy, asthma, and	rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and
many characteristics of immature mast cells.	This reporter assay measures	activation of the NFAT	signaling pathway in HMC-1	human mast cell line.	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of
	Activation of	transcription	through NFAT	response element in	immune cells (such	as mast cells).																							
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		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
	_	invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
,		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
		Exemplary human mast cells	mellitus, endocarditis,
		that may be used according to	meningitis, and Lyme Disease.
		these assays include the HMC-	
-		1 cell line, which is an	
		immature human mast cell line	
		established from the peripheral	

blood of a patient with mast cell leukemia, and exhibits many characteristics of	immature mast cells.	RANTES FMAT. Assays for	immunomodulatory proteins	that induce chemotaxis of T	cells, monocytes, and	eosinophils are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and
		Production of	RANTES in	endothelial cells	(such as human	umbilical vein	endothelial cells	(HUVEC))														-						
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		HMSKC04																										
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agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	
																														SEAP in Jurkat/IL4
																														1295
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	Highly preferred indications include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases			multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious		indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described
	Assays for the activation of	Nuclear Factor of Activated T	cells (NFAT) response element	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	NFAT transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn
promoter (antiCD3 co-stim)	Activation of	through NFAT	response element in	immune cells (such	as natural killer	cells).												-										
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Ve	erred	le neopl	ı as, for	ia, lymp	est, lung	, esopha	iver and	ther pre-	le benig	lisorders	nditions	nyperpla	or dyspla	ions alsc	sancytor	nbocyto	e, acute	mia (AL	multiple	t's lymp	granulon	atory bo	eutropei	riasis,	nmune	planted	šs,	ercoagul	•
ıder roliferati	s"). Pref	ns incluc	ers, such	, leukem	tate, brea	ıncreatic	brain, l	ancer. 0	ns inclue	erative of	lastic co	rample, l	ia, and/c	indicat	memia, 1	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	ytomas,	a, Burkit	arthritis, AIDS, granulomatous	disease, inflammatory bowel	sepsis, n	neutrophilia, psoriasis,	ion of in	s to trans	organs and tissues,	hemophilia, hypercoagulation,	111.4
et al., Proc Natl Acad Sci USA below under 85:6342-6346 (1988): "Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukoper	Hodgkin	lymphoc	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis,	disease,	disease, sepsis, neutropenia,	neutropł	suppression of immune	reactions to transplanted	organs a	hemoph	1: 1 1 - 1 - 11 think and a countileting
i USA	Jed led	De	n Cell	1999);	lou	pu	m m	993),	/hich	y	NK	•	s are			ells	ing to	NK-	human	ith	•			***					
Acad Sc 1988):	JExp N	(1995);	Biocher	1-1236 (r J Immu	1999); a	Biol Che	14293 (1	each of v	porated l	entirety.	e used	se assay	le (e.g.,	(CC)	an NK c	d accord	lude the	nich is a	Il line w	totoxic								
et al., Proc Natl Acad 85:6342-6346 (1988);	Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic	·							
et al., P	Aramb	182(3):	Boer et	Biol 31	Fraser	29(3):8	Yeseen	268(19	the con	are her	referen	cells th	accord	public	throug	Exemp	that ma	these a	YT cel	natural	cytolyt	activity.							
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347	HMSKC04				
347		1295	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
_				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
.00				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
	-			transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
-				Malm, Methods in Enzymol	suppressing a T cell-mediated
				216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications

include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma,	and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications	include neoplasms and cancers, such as, for example, leukemia, lymphoma,	melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia,
85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays	include the NK-YT cell line, which is a human natural killer cell line with cytolytic and	cytotoxic activity.			

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious Disease").	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as
	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions.
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
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	Evamplem account for	described below under
 	LACINDIAL J assays 101	"Trefactions Diseases" Highly
	transcription inrougn the AF1	injectious Disease). Tilginy
	response element that may be	preferred indications include
	used or routinely modified to	autoimmune diseases (e.g.,
	test AP1-response element	rheumatoid arthritis, systemic
 	activity of polypeptides of the	lupus erythematosis, multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below) and
	the invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
 -	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
-	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
 -	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety.	lung, colon, pancreatic,
	Human T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,

meta Prefe arthr aller; leuke Hody lymg plass mye gran infla seps imm trans tissu	CD28 embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An activating T cells. An embodiment of the invention includes a method for activating T cells. An activating T cells. An embodiment of the invention includes a method for activating T cells. An activating T cells. An includes a method for embodiment of the invention of to
line, which is an IL-2 and IL-4 responsive suspension-culture cell line.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
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	HMSKC04
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inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention	includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment	of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred	inflammation and inflammatory disorders. Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as	described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune	response, and suppressing a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., melanoma, renal	cell carcinoma, leukemia, lymphoma, and/or as described
test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J	Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem	3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4	responsive T cells.
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-		below under
		"Hyperproliferative
		Disorders"). Highly preferred
		indications include neoplasms
		and cancers, such as, for
		example, melanoma (e.g.,
		metastatic melanoma), renal
		cell carcinoma (e.g., metastatic
-		renal cell carcinoma),
		leukemia, lymphoma (e.g., T
		cell lymphoma), and prostate,
-		breast, lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		A highly preferred indication
		includes infection (e.g.,
	• •	AIDS, tuberculosis, infections
		associated with granulomatous
		disease, and osteoporosis,
		and/or as described below
		under "Infectious Disease"). A
		highly preferred indication is
		AIDS. Additional highly
		preferred indications include
		suppression of immune

				Total Control	reactions to transplanted
					organs and/or tissues, uveitis,
					psoriasis, and tropical spastic
					paraparesis. Preferred
					indications include blood
					disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMSKC04	1295	Activation of	Assays for the activation of	Highly preferred indications
347			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
- Sept.			immune cells (such	are well-known in the art and	under "Hyperproliferative
		•	as T-cells).	may be used or routinely	Disorders"). Highly preferred
			.(, marine	

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indications include neoplasms and cancers, such as, for example, leukemia, lymphoma	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkins lymphoma, Hodgkin"s disease),	melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for	example, hyperplasta, metaplasia, and/or dysplasia. Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies	(e.g., as described below), boosting a T cell-mediated	immune response, and suppressing a T cell-mediated immune response. Additional	preferred indications include inflammation and	inflammatory disorders.
modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) to regulate STAT transcription factors and modulate gene expression	involved in a wide variety of cell functions. Exemplary assays for transcription	element that may be used or routinely modified to test	GAS-response element activity of polypeptides of the	and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Matikainen et al., Blood	93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the	contents of each of which are herein incorporated by	reference in its entirety.
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Highly preferred indications include blood disorders (e.g.,	"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	intectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,
Exemplary human T cells, such as the SUPT cell line, that	assays are publicly available (e.g., through the ATCC).												-													
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diabetes mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.	Highly preferred indications	include blood disorders (e.g.,	as described below under		Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases			multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious		indications include neoplastic	
			Assays for the activation of	transcription through the	Nuclear Factor of Activated T	cells (NFAT) response element	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	NFAT transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	
			Activation of	transcription	through NFAT	response element in	immune cells (such	as T-cells).																	-					
			1295																											
			HMSKC04																	- Pro-										
				347	<u>.</u>									-																_

216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):118 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yessen et al., J Biol Chem 28(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.		Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,	and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also	include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis AIDS granulomatous	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation,
	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which	are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g.,	Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4	

					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMSKC04	1295	Activation of	Assays for the activation of	Highly preferred indications
347			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
21				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
	-			NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

85:6342-6346 (1988); Bl al., Virus Gnes 15(2):10 (1997); and Fraser et al., 29(3):838-844 (1999), th contents of each of whic herein incorporated by reference in its entirety. cells that may be used according to these assay, publicly available (e.g., through the ATCC). Exemplary human T cell may be used according to assays include the SUPT line, which is a suspensi culture of IL.2 and IL-4 responsive T cells.	85:6342-6346 (1988); Black et Disorders"). Highly preferred al., Virus Gnes 15(2):105-117 indications include neoplasms (1997); and Fraser et al., and cancers, such as melanoma renal cell	h are	s are	publicly available (e.g., preferred indications include through the ATCC).	Exemplary human T cells that disorders and pre-neoplastic may be used according to these conditions, such as, for		line, which is a suspension metaplasia, and/or dysplasia.		leukopenia, thrombocytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL)	plasmacytomas, multiple	myeloma, Burkitt's lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cumpression of immine
	85:6342-67 al., Virus (1997); and	contents of herein inco	cells that n	publicly available (e	Exemplary may be use	assays incl	line, which	responsive T cells.	-											

					reactions to transplanted
					organs, asthma and allergy.
	HMSKC04	1295	Activation of	Assays for the activation of	A highly preferred
347			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
	-			STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include
				antagonists of the invention)	neoplastic diseases (e.g.,
				include assays disclosed in	leukemia, lymphoma,
				Berger et al., Gene 66:1-10	melanoma, and/or as described
				(1998); Cullen and Malm,	below under
				Methods in Enzymol 216:362-	"Hyperproliferative
				368 (1992); Henthorn et al.,	Disorders"). Preferred

indications include neoplasms	oras and cancers, such as, leukemia,				-		J indications include benign			as, for example, hyperplasia,	in its metaplasia, and/or dysplasia.	be Preferred indications include	says anemia, pancytopenia,	,, leukopenia, thrombocytopenia,	Hodgkin's disease, acute		says plasmacytomas, multiple	, myeloma, Burkitt's lymphoma,	ure arthritis, AIDS, granulomatous		disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.	An additional preferred	indication is infaction (a & an
Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas	et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987	(1997); and Masuda et al., J	Biol Chem 275(38):29331-	29337 (2000), the contents of	each of which are herein	incorporated by reference in its	entirety. T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the SUPT cell line,	which is a suspension culture	of IL-2 and IL-4 responsive T	cells.									
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infectious disease as described	below under "Infectious				ay ay		oility of (e.g., an infectious disease as		odies and "Infectious Disease"),					atory genes. "Immune Activity", and	-					nt activity of sclerosis and/or as described		odies and immunodeficiencies (e.g., as	the	ide assays	disclosed in Berger et al., Gene	Cullen and	in Enzymol	992); Henthorn	
		Activation of Assays for the activation of		through NFKB NFKB response element are	response element in well-known in	immune cells (such be used or routinely modified	as EOL1 cells). to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Ber	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	TOLL OF THE OF IT AT
		1296 Activ	transe	thron	respo	immi	as E(-	•									_		-,-			
		HMTBI36														,													
			348																_										

85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	NFKB element to a repeorter	gene and binds to the NFKB	transcription factor, which is	upregulated by cytokines and	other factors. Exemplary	immune cells that may be used	according to these assays	include eosinophils such as the	human EOL-1 cell line of	eosinophils. Eosinophils are a	type of immune cell important	in the allergic responses; they	are recruited to tissues and	mediate the inflammtory	response of late stage allergic	reaction. Eol-1 is a human	eosinophil cell line.
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	HMTBI36	1296	Activation of	Kinase assay. Kinase assays,	A highly preferred
348			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for
			Signalling Pathway	transduction that regulate	increasing muscle cell survival
				glucose metabolism and cell	An alternative highly preferred
				survivial are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing muscle cell
		-		the ability of polypeptides of	survival. A preferred
				the invention (including	embodiment of the invention
				antibodies and agonists or	includes a method for
				antagonists of the invention) to	stimulating muscle cell
		•		promote or inhibit glucose	proliferation. In a specific
				metabolism and cell survival.	embodiment, skeletal muscle
				Exemplary assays for PI3	cell proliferation is stimulated.
	_			kinase activity that may be	An alternative highly preferred
				used or routinely modified to	embodiment of the invention
				test PI3 kinase-induced activity	includes a method for
				of polypeptides of the	inhibiting muscle cell
				invention (including antibodies	proliferation. In a specific
				and agonists or antagonists of	embodiment, skeletal muscle
				the invention) include assays	cell proliferation is inhibited.
			-	disclosed in Forrer et al., Biol	A preferred embodiment of
				Chem 379(8-9):1101-1110	the invention includes a
				(1998); Nikoulina et al.,	method for stimulating muscle
				Diabetes 49(2):263-271	cell differentiation. In a
				(2000); and Schreyer et al.,	specific embodiment, skeletal
				Diabetes 48(8):1662-1666	muscle cell differentiation is
			-	(1999), the contents of each of	stimulated. An alternative
			-	which are herein incorporated	highly preferred embodiment
				by reference in its entirety.	of the invention includes a

method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is	indications include disorders of the musculoskeletal system. Preferred indications include	neoplastic diseases (e.g., as described below under	"Hyperproliterative Disorders"), endocrine	disorders (e.g., as described below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular Disorders" and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred
Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC).	that may be used according to these assays include L6 cells.	cell line, isolated from primary cultures of rat thigh muscle,	that tuses to form multinucleated myotubes and	striated fibers after culture in differentiation media.											-				
							- 												

indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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	-																													

		neuropathy, vision impairment
-		(e.g., diabetic retinopathy and
		blindness), ulcers and impaired
		wound healing, infections
		(e.g., infectious diseases and
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	disorders as described in the
		"Infectious Diseases" section
		below, especially of the
		urinary tract and skin), carpal
		tunnel syndrome and
		Dupuytren's contracture).
		An additional highly preferred
		 indication is obesity and/or
		complications associated with
		obesity. Additional highly
		preferred indications include
		weight loss or alternatively,
		weight gain. Additional
		highly preferred indications are
		complications associated with
		insulin resistance.
		Additonal highly preferred
		indications are disorders of the
		musculoskeletal system
		including myopathies,
		muscular dystrophy, and/or as
		described herein.
-		Additional highly preferred
		indications include: myopathy,
		atrophy, congestive heart
		failure cachevia myxomas

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					Indianas, congenitai
					cardiovascular abnormalities,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease. Highly
					preferred indications include
					neoplasms and cancer, such as,
					rhabdomyoma,
					rhabdosarcoma, stomach,
-					esophageal, prostate, and
					urinary cancer. Preferred
					indications also include breast,
					lung, colon, pancreatic, brain,
					and liver cancer. Other
					preferred indications include
_					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as,
					hyperplasia, metaplasia, and/or
		3			dysplasia.
348	HMTBI36	1296	ICAM in OE19		
	HMTBI36	1296	SEAP in		
348			Senescence Assay		
	HMUAP70	1297	Activation of	Assays for the activation of	A preferred embodiment of
349			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method

			the invention (including	for stimulating (e o
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
	•		factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
		-	for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn's disease, multiple
			include assays disclosed in	sclerosis and/or as described
			Berger et al., Gene 66:1-10	below), immunodeficiencies
;			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
		-	368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional
			Black et al., Virus Genes	highly preferred indications
			12(2):105-117 (1997), the	include inflammation and
			content of each of which are	inflammatory disorders, and
			herein incorporated by	treating joint damage in
			reference in its entirety. T	patients with rheumatoid
			cells that may be used	arthritis. An additional highly
			according to these assays are	preferred indication is sepsis.
			publicly available (e.g.,	Highly preferred indications
			through the ATCC).	include neoplastic diseases
	Line		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,

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and/or as described below	under "Hyperproliterative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune
may be used according to these	assays include the CILL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.				***																					
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osteoporosis, and/or as	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma and proctate
(including antibodies and o		immunomodulation, regulate p		modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated s	immunity. Exemplary assays b		immunomodulatory proteins b	evaluate the production of in	cytokines, such as Interferon s	gamma (IFNg), and the	activation of T cells. Such h	assays that may be used or	routinely modified to test ii	<u>ب</u>			the	invention) include the assays n	disclosed in Miraglia et al., J	Biomolecular Screening 4:193- n	204 (1999); Rowland et al., b	"Lymphocytes: a practical "	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad e	Sci 856-22-32 (1998) Boehm

				of of Annu Doy Imminol	breast ling colon pancreatic
			,	et al., Allila INCV Illillialloi	Olcast, Iung, Coon, Panel Carre,
				15:/49-/95 (1997), and	esopnageal, stomacn, orain,
				Rheumatology (Oxford)	liver and urinary cancer. Other
		•		38(3):214-20 (1999), the	preferred indications include
				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
		1/11		reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMVBN46	1298	VEGF in SW480		
350					
351	HMWEB02	1299	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include neoplastic diseases
100					

	through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
	response element in	Site (GAS) response element	and/or as described below
	immune cells (such	are well-known in the art and	under "Hyperproliferative
	as T-cells).	may be used or routinely	Disorders"). Highly preferred
		modified to assess the ability	indications include neoplasms
		of polypeptides of the	and cancers, such as, for
	-	invention (including antibodies	example, leukemia, lymphoma
		and agonists or antagonists of	(e.g., T cell lymphoma,
		the invention) to regulate	Burkitt's lymphoma, non-
-		STAT transcription factors and	Hodgkins lymphoma,
		modulate gene expression	Hodgkin"s disease),
		involved in a wide variety of	melanoma, and prostate,
		cell functions. Exemplary	breast, lung, colon, pancreatic,
		assays for transcription	esophageal, stomach, brain,
		through the GAS response	liver and urinary cancer. Other
		element that may be used or	preferred indications include
		routinely modified to test	benign dysproliferative
		GAS-response element activity	disorders and pre-neoplastic
		of polypeptides of the	conditions, such as, for
		invention (including antibodies	example, hyperplasia,
		and agonists or antagonists of	metaplasia, and/or dysplasia.
		the invention) include assays	Preferred indications include
		disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
		66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
		Malm, Methods in Enzymol	lupus erythematosis, multiple
		216:362-368 (1992); Henthorn	sclerosis and/or as described
		et al., Proc Natl Acad Sci USA	below), immunodeficiencies
-		85:6342-6346 (1988);	(e.g., as described below),
		Matikainen et al., Blood	boosting a T cell-mediated
		93(6):1980-1991 (1999); and	immune response, and
		Henttinen et al., J Immunol	suppressing a T cell-mediated

		155(10):4582-4587 (1995), the	immune response. Additional
		contents of each of which are	preferred indications include
		herein incorporated by	inflammation and
		reference in its entirety.	inflammatory disorders.
		Exemplary mouse T cells that	Highly preferred indications
		may be used according to these	include blood disorders (e.g.,
	**	assays are publicly available	as described below under
		(e.g., through the ATCC).	"Immune Activity", "Blood-
		Exemplary T cells that may be	Related Disorders", and/or
		used according to these assays	"Cardiovascular Disorders"),
		include the CTLL cell line,	and infection (e.g., viral
		which is a suspension culture	infections, tuberculosis,
		of IL-2 dependent cytotoxic T	infections associated with
		cells.	chronic granulomatosus
,			disease and malignant
			osteoporosis, and/or an
			infectious disease as described
			below under "Infectious
			Disease"). An additional
			preferred indication is
			idiopathic pulmonary fibrosis.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			acute lymphocytic anemia
			(ALL), plasmacytomas,
			multiple myeloma, arthritis,
	-1		AIDS, granulomatous disease,
		9-19	inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.				A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes allergy. A highly preferred indication includes rhinitis. Additional highly preferred indications include inflammation and inflammation and inflammatory disorders.
				IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cells polarization, and/or mediate humoral or
	IgG in Human B cells SAC	IL-12 in Human B cells SAC	IL-13 in HMC	Production of IL-4
	1299	1299	1300	1300
	HMWEB02	HMWEB02	HMWF002	HMWF002
	351	351	352	352

		cell-mediated immunity.	Highly preferred indications
		Exemplary assays that test for	include neoplastic diseases
		immunomodulatory proteins	(e.g., leukemia, lymphoma,
		evaluate the production of	melanoma, and/or as described
		cytokines, such as IL-4, and	below under
		the stimulation of immune	"Hyperproliferative
		cells, such as B cells, T cells,	Disorders"). Preferred
		macrophages and mast cells.	indications include neoplasms
		Such assays that may be used	and cancers, such as, for
		or routinely modified to test	example, leukemia, lymphoma,
		immunomodulatory activity of	melanoma, and prostate,
		polypeptides of the invention	breast, lung, colon, pancreatic,
	www.	(including antibodies and	esophageal, stomach, brain,
		agonists or antagonists of the	liver and urinary cancer. Other
		invention) include the assays	preferred indications include
		disclosed in Miraglia et al., J	benign dysproliferative
		Biomolecular Screening 4:193-	disorders and pre-neoplastic
		204 (1999); Rowland et al.,	conditions, such as, for
		"Lymphocytes: a practical	example, hyperplasia,
		approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
		(2000); Gonzalez et al., J Clin	Preferred indications include
371		Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
		Yssel et al., Res Immunol	described below under
		144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
		et al., Nat Immunol 1(3):257-	Related Disorders", and/or
		261 (2000); and van der Graaff	"Cardiovascular Disorders").
		et al., Rheumatology (Oxford)	Preferred indications include
		38(3):214-220 (1999), the	autoimmune diseases (e.g.,
		contents of each of which are	rheumatoid arthritis, systemic
	-	herein incorporated by	lupus erythematosis, multiple
		reference in its entirety.	sclerosis and/or as described

				Human T cells that may be	below) and
				used according to these assays	immunodeficiencies (e.g., as
				may be isolated using	described below). Preferred
~				techniques disclosed herein or	indications include anemia,
				otherwise known in the art.	pancytopenia, leukopenia,
				Human T cells are primary	thrombocytopenia, Hodgkin's
				human lymphocytes that	disease, acute lymphocytic
				mature in the thymus and	anemia (ALL),
				express a T cell receptor and	plasmacytomas, multiple
				CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
	•			cells mediate humoral or cell-	arthritis, AIDS, granulomatous
				mediated immunity and may	disease, inflammatory bowel
				be preactivated to enhance	disease, sepsis, neutropenia,
				responsiveness to	neutrophilia, psoriasis,
				immunomodulatory factors.	suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HMWGY65	1301	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
353			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
))			Signaling Pathway.	transduction that regulate cell	described below under
)	proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				The state of the s	

"Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection	(e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional	highly preferred indications include inflammation and	inflammatory disorders. Highly preferred indications	also include neoplastic diseases (e.g., leukemia,	lymphoma, and/or as described below under	"Hyperproliferative	indications include neoplasms	and cancers, such as, leukemia, lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or	antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation,	Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to	test JNK and p38 kinase- induced activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include the assays	disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):3/-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999); the contents of each of which	are herein incorporated by	reference in its entirety. T
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preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,	meningius, and Lyme Disease.
according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
	1301
	HMWGY65
	353

entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or antibodies and agonists or promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase and n38 kinase-induced a kinase assays for signal ambodiment of the invention and agonists of the invention includes a method for stimulating endothelial cell proliferation, activation, and activity that may be used or and n38 kinase-induced A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation, activation, and activity that may be used or and n38 kinase-induced A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting promote or inhibit cell proliferation, activation, and activity that may be used or and n38 kinase-induced A highly preferred embodiment of the invention includes a method for inhibiting embodiment of the invention includes a method for inhibiting embodiment of the invention includes a method for inhibiting proliferation, activation, and activity that may be used or method for inhibiting endothelial cell provides an enthod for inhibiting proliferation, activation, and activity that may be used or method for inhibiting endothelial cell provides a method for invention includes a method for inhibiting proliferation. An alternative includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.
entirety. with SID SEAP act after 72 h human he carcinom HB-8065 Science. contents incorpora	IFNg in Human T- cell 2B9	on of lial Cell NK g Pathway.
	1301 IF	1301 Signature 1301
	HMWGY65	HMWGY65
	353	353

embodiment of the invention includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac
activity of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular
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permeability, vascular tone, and immune cell extravasation.	hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as	described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as
	permeability, vascular tone, and immune cell extravasation.			

well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,
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ischemia reperfusion injury, rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple
										·																			

sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1302
	HNEAC05
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		A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	,	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the
	MCP-1 in HUVEC	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1302	1302
	HNEAC05	HNEAC05
	354	354

Disorders", and/or "Cardiovascular Disorders"),	Highly preferred indications include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,
function of growth-related genes in many cell types.	Exemplary assays for transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and
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				additional preferred indication
				is infection (e.g., an infectious
				uisease as described below under "Infectious Disease").
HNEEB45	1303	Activation of	Assays for the activation of	A highly preferred indication
		transcription	transcription through the	is obesity and/or complications
		through cAMP	cAMP response element are	associated with obesity.
		response element	well-known in the art and may	Additional highly preferred
		(CRE) in pre-	be used or routinely modified	indications include weight loss
		adipocytes.	to assess the ability of	or alternatively, weight gain.
			polypeptides of the invention	An additional highly preferred
			(including antibodies and	indication is diabetes mellitus.
			agonists or antagonists of the	An additional highly preferred
			invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other
			3T3-L1/CRE reporter assay	diseases and disorders as
			may be used to identify factors	described in the "Renal
			that activate the cAMP	Disorders" section below),
			signaling pathway. CREB	diabetic neuropathy, nerve
			plays a major role in	disease and nerve damage
		100	adipogenesis, and is involved	(e.g., due to diabetic
			in differentiation into	neuropathy), blood vessel
			adipocytes. CRE contains the	blockage, heart disease, stroke,
			binding sequence for the	impotence (e.g., due to diabetic
			transcription factor CREB	neuropathy or blood vessel
			(CRE binding protein).	blockage), seizures, mental
			Exemplary assays for	confusion, drowsiness,

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described
is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1303
	HNEEB45
	355

Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	immune response, and
 Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
 Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below
assays include the CTLL cell	under "Hyperproliferative
line, which is an IL-2	Disorders"). Additionally,
dependent suspension culture	highly preferred indications
of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,
	leukemia, lymphoma,
	melanoma, glioma (e.g.,
	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative

	·					disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
2147				,		myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication
355	. 22	HNEEB45	1303	Activation of transcription through NFKB	Assays for the activation of transcription through the NFKB response element are	disease as described below under "Infectious Disease"). Highly preferred indications include asthma, allergy,

indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease").	immunological disorders.	inflammation and	inflammatory disorders (e.g.,	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below).													
be used or routinely modified	to assess the ability of	nolvnentides of the invention	finchiding antihodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of
immine cells (such	as FOL1 cells)	" TOTI (2012):						100							-								-							

	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and
rety. r assay ases in from a ent in the seorter VFKB nich is he used ary be used ary he used ary ary and ills are a apportant es; they and ry and man	Assays for measuring expression of VCAM are well- known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention in (including antibodies and
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1303
	HNEEB45
	355

agonists or antagonists of the inflammatory disorders, invention) to regulate VCAM expression. For example, repulation of cell surface and the upregulation of cells are cells that line blood cells are cells that line blood are cells	od
agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-I expresssion in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in	agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-I expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels, thus VCAM expression plays a role in

				inflammatory responses.	
	HNEEB45	1303	Caspase		
355			(+paclitaxel) in SW480		
	HNFFC43	1304	Regulation of	Assays for the regulation of	A highly preferred indication
356			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
		•		DMEF1 response element in a	diseases and disorders as
				reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),
_				promoter) and to regulate	diabetic neuropathy, nerve
				insulin production. The	disease and nerve damage
				DMEF1 response element is	(e.g., due to diabetic
				present in the GLUT4	neuropathy), blood vessel
				promoter and binds to MEF2	blockage, heart disease, stroke,
				transcription factor and another	impotence (e.g., due to diabetic
				transcription factor that is	neuropathy or blood vessel
				required for insulin regulation	blockage), seizures, mental
				of Glut4 expression in skeletal	confusion, drowsiness,
				muscle. GLUT4 is the primary	nonketotic hyperglycemic-
				insulin-responsive glucose	hyperosmolar coma,
				transporter in fat and muscle	cardiovascular disease (e.g.,
				tissue. Exemplary assays that	heart disease, atherosclerosis,
				may be used or routinely	microvascular disease,

modified to test for DMEF1	hypertension, stroke, and other
response element activity (in	diseases and disorders as
adipocytes and pre-adipocytes)	described in the
by polypeptides of the	"Cardiovascular Disorders"
invention (including antibodies	section below), dyslipidemia,
and agonists or antagonists of	endocrine disorders (as
the invention) include assays	described in the "Endocrine
disclosed in Thai, M.V., et al., J	Disorders" section below),
Biol Chem, 273(23):14285-92	neuropathy, vision impairment
(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
Chem, 275(21):16323-8	blindness), ulcers and impaired
(2000); Liu, M.L., et al., J Biol	wound healing, and infection
Chem, 269(45):28514-21	(e.g., infectious diseases and
(1994); "Identification of a 30-	disorders as described in the
 base pair regulatory element	"Infectious Diseases" section
and novel DNA binding	below, especially of the
protein that regulates the	urinary tract and skin). An
human GLUT4 promoter in	additional highly preferred
 transgenic mice", J Biol Chem.	indication is obesity and/or
2000 Aug 4;275(31):23666-73;	complications associated with
Berger, et al., Gene 66:1-10	obesity. Additional highly
(1988); and, Cullen, B., et al.,	preferred indications include
Methods in Enzymol.	weight loss or alternatively,
216:362–368 (1992), the	weight gain. Additional highly
contents of each of which is	preferred indications are
herein incorporated by	complications associated with
reference in its entirety.	insulin resistance.
Adipocytes and pre-adipocytes	
that may be used according to	
these assays are publicly	
available (e.g., through the	!

				ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
356	HNFFC43	1304	Proliferation of immune cells (such as the HMC-1 human mast cell line)	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp.,	Highly preferred indications include asthma, allergy, mastocytosis (a rare, heterogeneous disorder characterized by excessive accumulation of mast cells, and their proliferation and action in the skin, central nervous system, and other organs). Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), infection (e.g., as described

below under "Infectious	Disease"), autoimmune	arthritis, systemic lubus	erythematosis, multiple	sclerosis and/or as described	below), and	immunodeficiencies (e.g., as	described below).																						
Madison, WI, USA) can be	used to measure the number of	quantitation of the ATP	present which signals the	presence of metabolically	active cells. Mast cells are	found in connective and	mucosal tissues throughout the	body. Mast cell activation (via	immunoglobulin E -antigen,	promoted by T helper cell type	2 cytokines) is an important	component of allergic disease.	Dysregulation of mast cell	apoptosis may play a role in	allergic disease and mast cell	tumor survival. Mast cell lines	that may be used according to	these assays are publicly	available and/or may be	routinely generated.	Exemplary mast cells that may	be used according to these	assays include HMC-1, which	is an immature human mast	cell line established from the	peripheral blood of a patient	with mast cell leukemia, and	exhibits many characteristics	of immature mast cells.
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	HNFFC43	1304	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
356			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
	***			apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
			•	the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
				(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
			-	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
				Symp 64:29-48 (1999); Chang	below under
				and Karin, Nature	"Hyperproliferative
ļ				410(6824):37-40 (2001); and	Disorders"). Highly preferred

				Cobb MH, Prog Biophys Mol	indications include neoplasms
				Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
		, .		the contents of each of which	lymphoma, prostate, breast,
				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
		.,		cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
		-		activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HNFFC43	1304	Regulation of	Assays for the regulation of	A highly preferred
356			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication

associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve		(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment
modified to assess the ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	transcription of Malic Enzyme,	a key enzyme in lipogenesis.	Malic enzyme is involved in	lipogenesisand its expression is	stimulted by insulin. ME	promoter contains two direct	repeat (DR1)- like elements	MEp and MEd identified as	putative PPAR response	elements. ME promoter may	also responds to AP1 and other	transcription factors.	Exemplary assays that may be	used or routinely modified to	test for regulation of	transcription of Malic Enzyme	(in adipoocytes) by	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in: Streeper, R.S., et	al., Mol Endocrinol,	12(11):1778-91 (1998);	Garcia-Jimenez, C., et al., Mol	Endocrinol, 8(10):1361-9
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																					-								

				(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
				Biol Chem, 274(25):17997-	blindness), ulcers and impaired
				8004 (1999); Ijpenberg, A., et	wound healing, and infection
				al., J Biol Chem,	(e.g., infectious diseases and
-				272(32):20108-20117 (1997);	disorders as described in the
				Berger, et al., Gene 66:1-10	"Infectious Diseases" section
				(1988); and, Cullen, B., et al.,	below, especially of the
				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HNFFC43	1304	SEAP in		
356			Senescence Assay		
	HNFIU96	1305	Activation of	This reporter assay measures	Highly preferred indications
357			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
		-		production. Assays for the	inflammation and

	activation of transcription	inflammatory disorders.
	through the Nuclear Factor of	Preferred indications also
	Activated T cells (NFAT)	include blood disorders (e.g.,
	response element are well-	as described below under
 	known in the art and may be	"Immune Activity", "Blood-
	used or routinely modified to	Related Disorders", and/or
 	assess the ability of	"Cardiovascular Disorders").
	polypeptides of the invention	Preferred indications include
-	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
 	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
 	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
 	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
 	may be used or routinely	prostate, breast, lung, colon,
 	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
 	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
 	66:1-10 (1998); Cullen and	dysproliferative disorders and
 	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include

				et al., Int J Biochem Cell Biol	anemia, pancytopenia,
				31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
				et al., J Immunol	leukemias, Hodgkin's disease,
· -				165(12):7215-7223 (2000);	acute lymphocytic anemia
				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
· · · · ·				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HNFJF07	1306	Regulation of	Assays for the regulation of	A highly preferred indication
358			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic

polype (includagonis) agonis invent DMEH report contain promo insulity DMEH present promo transcriptory of Glumusch insulity transcriptory insulity transport insulity transport insulity transport insulity transport invent adipocal property inventory by polyinventory inventory inventor	including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies	retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease, atherosclerosis, microvascular disease, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, section below), dyslipidemia,
the in	the invention) include assays	described in the "Endocrine
disclo Biol C	disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998): Mora, S., et al., 1 Biol	Disorders" section below), neuropathy, vision impairment

Chem, 275(21):16323-8 Chom, 269(45):2851-41 Chem, 269(45):2851-2851 Chem, 269(45):2851 Chem, 269(45)

				the invention) include assays	hypertension, stroke, and other
				disclosed in: Friedrichsen BN,	diseases and disorders as
				et al., Mol Endocrinol,	described in the
				15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
				MA, et al., Endocrinology,	section below), dyslipidemia,
				139(4):1494-9 (1998); Hugl	endocrine disorders (as
				SR, et al., J Biol Chem 1998	described in the "Endocrine
				Jul 10;273(28):17771-9	Disorders" section below),
				(1998), the contents of each of	neuropathy, vision impairment
				which is herein incorporated	(e.g., diabetic retinopathy and
				by reference in its entirety.	blindness), ulcers and impaired
				Pancreatic cells that may be	wound healing, and infection
				used according to these assays	(e.g., infectious diseases and
				are publicly available (e.g.,	disorders as described in the
				through the ATCC) and/or	"Infectious Diseases" section
				may be routinely generated.	below, especially of the
				Exemplary pancreatic cells that	urinary tract and skin), carpal
				may be used according to these	tunnel syndrome and
				assays include rat INS-1 cells.	Dupuytren's contracture). An
				INS-1 cells are a semi-	additional highly preferred
				adherent cell line established	indication is obesity and/or
				from cells isolated from an X-	complications associated with
	-			ray induced rat transplantable	obesity. Additional highly
				insulinoma. These cells retain	preferred indications include
				characteristics typical of native	weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asfari	complications associated with
	** **			et al. Endocrinology 1992	insulin resistance.
				130:167.	
HNFJF07		306	Activation of	Assays for the activation of	A preferred embodiment of

the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative meferred embodiment of the	invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),	include autoimmune diseases include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in
transcription through the Serum Response Element (SRE) are well-known in the art and may be used or	the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response	factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or	activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by
through serum response element in immune cells (such	as 1-cells).			
358				

myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage
	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is
	Stimulation of insulin secretion from pancreatic beta cells.
	1306
	HNFJF07
	358

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(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuvtren's contracture).
upregulated by glucose and also by certain	proteins/peptides, and	disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated Exemplary
						-				,																			
			313																										

			(including antibodies and	sclerosis and/or as described
			agonists or antagonists of the	below) and
			invention) include assays	immunodeficiencies (e.g., as
			disclosed in Berger et al., Gene	described below). Additional
		W	66:1-10 (1988); Cullen and	highly preferred indications
			Malm, Methods in Enzymol	include inflammation and
			216:362-368 (1992); Henthorn	inflammatory disorders.
			et al., Proc Natl Acad Sci USA	Highly preferred indications
			85:6342-6346 (1988);	also include neoplastic
			Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
			272(49):30806-30811 (1997);	lymphoma, and/or as described
			Chang et al., Mol Cell Biol	below under
			18(9):4986-4993 (1998); and	"Hyperproliferative
			Fraser et al., Eur J Immunol	Disorders"). Highly preferred
			29(3):838-844 (1999), the	indications include neoplasms
			contents of each of which are	and cancers, such as, leukemia,
			herein incorporated by	lymphoma, prostate, breast,
			reference in its entirety. T	lung, colon, pancreatic,
			cells that may be used	esophageal, stomach, brain,
			according to these assays are	liver, and urinary cancer. Other
-			publicly available (e.g.,	preferred indications include
			through the ATCC).	benign dysproliferative
	-		Exemplary mouse T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
			assays include the CTLL cell	example, hyperplasia,
			line, which is an IL-2	metaplasia, and/or dysplasia.
			dependent suspension-culture	Preferred indications include
			cell line with cytotoxic	arthritis, asthma, AIDS,
			activity.	allergy, anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute

lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	1307 Activation of This reporter assay measures transcription activation of the GATA-3 include allergy, asthma, and through GATA-3 in mast cells (such as mast cells). cells has been linked to production. Assays for the activation of transcription include blood disorders (e.g., an infectious Disease "Infectious Disease"), and activation of transcription inflammatory disorders. Through the GATA3 response element are well-known in the activation of transcription include blood disorders (e.g., art and may be used or "Immune Activity", "Bloodthe invention (including and agonists or regulate GATA3 transcription including autoimnune diseases (e.g., regulate GATA3 transcription in the unwantoid arthritis, systemic factors and modulate
	1307
	HNFJH45
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immunodeficiencies (e.g., as described below). Preferred inclinations include neonlastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	W. Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted
development. Exemplary assays for transcription	through the GALA3 response element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).
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organs and tissues, hemophilia, hypercoagulation, diabetes IC-mellitus, endocarditis, meningitis, and Lyme Disease. ine tral	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
	1307
	HNFJH45
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		involved in	immunodeficiencies (e.g., as
		imminomodulatory functions.	described below). Preferred
		Exemplary assays for	indications include neoplastic
		transcription through the	diseases (e.g., leukemia,
		NFAT response element that	lymphoma, melanoma,
		may be used or routinely	prostate, breast, lung, colon,
•		modified to test NFAT-	pancreatic, esophageal,
		response element activity of	stomach, brain, liver, and
		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred
 ÷-		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	_	et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	48.14	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted

organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention
publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase
	Endothelial Cell Apoptosis
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		endothelial cells. An	the alternative highly preferred	ays embodiment of the invention	BS includes a method for	(000); inhibiting (e.g., decreasing)		san A highly preferred		6); includes a method for	ich	_	embodiment of the invention		ssays inhibiting angiogenesis. A			Ils method for reducing cardiac	to	ne highly preferred embodiment	of the invention includes a			olved preferred indications include		described below under	"Hyperproliferative	ie, Disorders"), and disorders of	ation. the cardiovascular system	
apoptosis activity of	polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	

heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders")	Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the	arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity
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to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer,	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors,	telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma,	haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metanlasia and/or dyspesia	Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory

vasculitides, Reynaud"s disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,
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		-																		-									

age-related macular degeneration, and treatment /prevention of endometriosis	and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and	vascular disease. Preferred indications include blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such	as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.

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A preferred embodiment of the invention includes a method for inhibiting (e.g.,	reducing) TNF alpha production. An alternative	preferred embodiment of the	invention includes a method for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and
Assays for the activation of transcription through the Serum Response Element	(SRE) are well-known in the art and may be used or	routinely modified to assess	the ability of polypeptides of the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are
Activation of transcription through serum	response element in immune cells (such	as T-cells).																								
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treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Lodalin's disorder accentications include	lymphocytic anemia (ALL),
herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.	
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					plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
361	HNGAP93	1309	IFNg in Human T-cell 2B9		
361	HNGAP93	1309	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke

	the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha ion) to production. Preferred indications include blood disorders (e.g., as described below under "Immune
modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved
	transcription through serum response element in immune cells (such as natural killer cells).
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		in growth and upregulate the	e the	Activity", "Blood-Related
		function of growth-related	ted	Disorders", and/or
		genes in many cell types.	·S	"Cardiovascular Disorders"),
		Exemplary assays for		Highly preferred indications
		transcription through the SRE	e SRE	include autoimmune diseases
		that may be used or routinely	tinely	(e.g., rheumatoid arthritis,
	_	modified to test SRE activity	tivity	systemic lupus erythematosis,
		of the polypeptides of the	Je	Crohn"s disease, multiple
		invention (including antibodies	ibodies	sclerosis and/or as described
		and agonists or antagonists of	ists of	below), immunodeficiencies
		the invention) include assays	ssays	(e.g., as described below),
		disclosed in Berger et al., Gene	ene	boosting a T cell-mediated
		66:1-10 (1998); Cullen and		immune response, and
		Malm, Methods in Enzymol	/mol	suppressing a T cell-mediated
		216:362-368 (1992); Henthorn	enthorn	immune response. Additional
		et al., Proc Natl Acad Sci USA	ci USA	highly preferred indications
	-	85:6342-6346 (1988); Benson	Senson	include inflammation and
		et al., J Immunol 153(9):3862-):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	et al.,	treating joint damage in
		Virus Genes 12(2):105-117	117	patients with rheumatoid
		(1997), the content of each of	ach of	arthritis. An additional highly
		which are herein incorporated	orated	preferred indication is sepsis.
		by reference in its entirety. T	ety. T	Highly preferred indications
		cells that may be used		include neoplastic diseases
		according to these assays are	/s are	(e.g., leukemia, lymphoma,
		publicly available (e.g.,		and/or as described below
		through the ATCC).		under "Hyperproliferative
		Exemplary T cells that may be	may be	Disorders"). Additionally,
		used according to these assays	assays	highly preferred indications
		include the NK-YT cell line,	line,	include neoplasms and
!		which is a human natural killer		cancers, such as, for example,

		cell line with cytolytic and	leukemia, lymphoma,
			molonomo diomo (e a
		cytotoxic activity.	incianolna, gnoma (c.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
		-	lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
	2-3		Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
	±481†		lymphocytic anemia (ALL),
	-		plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
	•		disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
	-		reactions to transplanted
			organs and tissues, hemophilia,
			hypercoagulation, diabetes
			mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and

					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
363	HNGBT31	1311	TNFa in Human T-cell 2B9		
	HNGBT31	1311	Activation of	Assays for the activation of	Highly preferred indications
363			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
		-		(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases

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eukemia,	as describe		ē	ly preferred	e neoplasm	as, for	na, renal ce	nia,	ostate,	ı, pancreatic	ch, brain,	ancer. Othe	ons include	ative	neoplastic	s, for	ısia,	· dysplasia.	ons also	ancytopenia	bocytopeni	e, acute	iia (ALL),	nultiple	's lymphon	anulomato	tory bowel	utropenia,	iasis,	coagulation
(e.g., melanoma, leukemia,	lymphoma, and/or as described	under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,
(e.g., m	Iymphc	below under	"Hyper	Disord	indicat	and car	examb	carcino	lymphc	breast,	esopha	liver ar	preferr	benign	disorde	conditi	examp	metapl	Preferr	include	leukop	Hodgk	lymphe	plasma	myelor	arthriti	disease	disease	neutro	hemop
66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4, that may	be used according to these	assays are publicly available	(e.g., through the ATCC).															
66:1-10	Malm, N	216:362	et al., Pr	85:6342	al., Viru	(1997);	29(3):83	contents	herein ii	referenc	Exempl	snch as	be used	assays a	(e.g., th	,														
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							<i>31.</i>																							
	. 84																												,	<u></u>

364	HNGDG40	1312	Proliferation of preadipose cells (such as 3T3-L1 cells)	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the Cell Titer-Gloô Luminescent Cell Viability	diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
				Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed	

	HNGDG40	1312	Activation of	through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety. Kinase assay. JNK and p38	A highly preferred
364			Endothelial Cell p38 or JNK Signaling Pathway.	kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of	embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of
				the invention) include the assays disclosed in Forrer et	endonnellal cells. An alternative highly preferred

		al Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
	-	410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	inhibiting (e.g., decreasing) the
		used according to these assays	activation of and/or
		are publicly available (e.g.,	inactivating endothelial cells.
		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
		(HUVEC), which are	embodiment of the invention
		endothelial cells which line	includes a method for
		venous blood vessels, and are	inhibiting angiogenesis. A
		involved in functions that	highly preferred embodiment
The state of the s		include, but are not limited to,	of the invention includes a
		angiogenesis, vascular	method for reducing cardiac
		permeability, vascular tone,	hypertrophy. An alternative
		and immune cell extravasation.	highly preferred embodiment
			of the invention includes a
			method for inducing cardiac
			hypertrophy. Highly

preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative	Disorders), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertronby, myocardial	infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders").	Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels	such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that

stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	done and this and distance one
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as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis,	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s	pnenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis,	lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease	and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured	tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions),	implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis,	cerebrovascular disease, renal diseases such as acute renal failure, and osteonorosis
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		-					

Additional highly preferred indications include stroke.	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include
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					inflammation and
					inflammatory disorders (such
					as acute and chronic
	10-				inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HNGDJ72	1313	Activation of	Kinase assay. Kinase assays,	A highly preferred
365			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
		-		inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment

	50	Se	used vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", and/or "Blood-Related Disorders", immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),
1110 (1998); Le Marchand- Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999);	Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999);	are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used.	according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.

described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the
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		- Village				-						,																		

-		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below),
		neuropathy, vision impairment
•		blindness), ulcers and impaired
		wound healing, infection (e.g.,
		infectious diseases and
***		disorders as described in the
		"Infectious Diseases" section
		below (particularly of the
		urinary tract and skin). An
		additional highly preferred
		indication is obesity and/or
		complications associated with
		obesity. Additional highly
		preferred indications include
	 <u> </u>	weight loss or alternatively,
	 	weight gain. Additional
		highly preferred indications are
		complications associated with
	 _	insulin resistance.
		Additional highly preferred
		indications are disorders of the
		musculoskeletal systems
		including myopathies,
		muscular dystrophy, and/or as
		described herein.
		Additional highly preferred

pe ye						indications include,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IA-A production and increases IA-A production and increases						hypertension, coronary artery
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A moduction of Increases						disease, dyslipidemia,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A moduction (In A plane as In A moduction of Increases).						gallstones, osteoarthritis,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and have a local production and have a						degenerative arthritis, eating
HNGD172 I313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and individual productio				0		disorders, fibrosis, cachexia,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A production and increases						and kidney diseases or
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A production (In A plays a						disorders. Preferred
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A moduction (IAA palays a						indications include neoplasms
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases for broad region and increases and the production and increases and the production and increases and the production and increases are production and increases and the production and increases are production and increases and the production and increases are production and increases and the production and increases are production and increases and the production and increases are production and increa						and cancer, such as,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A moduction (IAA) allows a						lymphoma, leukemia and
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases In A production and increases						breast, colon, and kidney
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A production and increases In A production and increases						cancer. Additional preferred
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases		-				indications include melanoma,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases and below as a moduction of the pays as						prostate, lung, pancreatic,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases to A production (ItA plays a						esophageal, stomach, brain,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases laA production (laA plays a						liver, and urinary cancer.
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases In A production (In A plays a						Highly preferred indications
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a						include lipomas and
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a						liposarcomas. Other preferred
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a						indications include benign
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a		•				dysproliferative disorders and
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a						pre-neoplastic conditions, such
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a						as, for example, hyperplasia,
HNGDJ72 1313 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases						metaplasia, and/or dysplasia.
by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases		HNGDJ72	1313	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
·	5				by T cells and has strong	embodiment of the invention
•					effects on B cells. IL-6	includes a method for
<u> </u>					participates in IL-4 induced	stimulating (e.g., increasing)
					IgE production and increases	IL-6 production. An alternative
					IgA production (IgA plays a	highly preferred embodiment

		role in mucosal immunity).	of the invention includes a
		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
		Deregulated expression of IL-6	reducing) IL-6 production. A
		has been linked to autoimmune	highly preferrred indication is
		disease, plasmacytomas,	the stimulation or enhancement
		myelomas, and chronic	of mucosal immunity. Highly
		hyperproliferative diseases.	preferred indications include
		Assays for immunomodulatory	blood disorders (e.g., as
		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
	-	factors, and hormones are well	described below under
		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
<u>.</u>		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and

activities Such assays that	inflammatorv
detailer bear about bear and an anning to	discussion Additional Links
may be used or routinely	disorders. Additional nighty
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative
204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lymphocytes: a practical	indications include neoplasms
approach" Chapter 6:138-160	and cancers, such as, myeloma,
 (2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
 (1997), the contents of each of	prostate, breast, lung, colon,
which are herein incorporated	pancreatic, esophageal,
 by reference in its entirety.	stomach, brain, liver and
Human dendritic cells that may	urinary cancer. Other preferred
 be used according to these	indications include benign
assays may be isolated using	dysproliferative disorders and
techniques disclosed herein or	pre-neoplastic conditions, such
otherwise known in the art.	as, for example, hyperplasia,
 Human dendritic cells are	metaplasia, and/or dysplasia.
 antigen presenting cells in	Preferred indications include
suspension culture, which,	anemia, pancytopenia,
when activated by antigen	leukopenia, thrombocytopenia,
and/or cytokines, initiate and	Hodgkin's disease, acute
 upregulate T cell proliferation	lymphocytic anemia (ALL),
and functional activities.	multiple myeloma, Burkitt's

lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as
	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T
	Production of MIP1alpha
	1313
	HNGDJ72
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	Related Disorders", and/or "Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,
cell differentiation. Exemplary assays that test for	immunomodulatory proteins evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, JR Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of
					-																							
·																												

			which are herein incorporated	meningitis, Lyme Disease,
			by reference in its entirety. Himan dendritic cells that may	asthma, and allergy. Preferred indications also
			be used according to these	include neoplastic diseases
			assays may be isolated using	(e.g., leukemia, lymphoma,
			techniques disclosed herein or	and/or as described below
			otherwise known in the art.	under "Hyperproliferative
			Human dendritic cells are	Disorders"). Highly preferred
			antigen presenting cells in	indications include neoplasms
			suspension culture, which,	and cancers, such as, leukemia,
			when activated by antigen	lymphoma, prostate, breast,
			and/or cytokines, initiate and	lung, colon, pancreatic,
			upregulate T cell proliferation	esophageal, stomach, brain,
			and functional activities.	liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
 HNGDJ72	1313	Production of TNF	TNFa FMAT. Assays for	A highly preferred
		alpha by dendritic	immunomodulatory proteins	embodiment of the invention
		cells	produced by activated	includes a method for
 			macrophages, T cells,	inhibiting (e.g., decreasing)
			fibroblasts, smooth muscle,	TNF alpha production. An
			and other cell types that exert a	alternative highly preferred
			wide variety of inflammatory	embodiment of the invention
			and cytotoxic effects on a	includes a method for
			variety of cells are well known	stimulating (e.g., increasing)
			in the art and may be used or	TNF alpha production.
			routinely modified to assess	Highly preferred indications

include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases	systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies	(e.g., as described below), boosting a T cell-mediated immune response, and	immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and		include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary	immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa),	and the induction or inhibition of an inflammatory or cytotoxic response. Such	assays that may be used of routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593

include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
(1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of	which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are	antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	

					cardiac reperfusion injury, and asthma and allergy. An
				•	additional preferred indication
					is infection (e.g., an infectious
				,	disease as described below
					under "Infectious Disease").
	HNGDJ72	1313	Production of	Endothelial cells, which are	Highly preferred indications
365			ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and
			umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
			endothelial cells	permeability, vascular tone,	indications include
			(HUVEC))	and immune cell extravasation.	inflammation and
		•	`	Exemplary endothelial cells	inflammatory disorders,
				that may be used in ICAM	immunological disorders,
				production assays include	neoplastic disorders (e.g.
				human umbilical vein	cancer/tumorigenesis), and
				endothelial cells (HUVEC),	cardiovascular disorders (such
				and are available from	as described below under
				commercial sources. The	"Immune Activity", "Blood-
				expression of ICAM (CD54),a	Related Disorders",
				intergral membrane protein,	"Hyperproliferative Disorders"
			13-1	can be upregulated by	and/or "Cardiovascular
				cytokines or other factors, and	Disorders"). Highly preferred
				ICAM expression is important	indications include neoplasms
				in mediating immune and	and cancers such as, for
				endothelial cell interactions	example, leukemia, lymphoma,
				leading to immune and	melanoma, renal cell
				inflammatory responses.	carcinoma, and prostate,
				Assays for measuring	breast, lung, colon, pancreatic,
				expression of ICAM-1 are	esophageal, stomach, brain,

liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include immunological and inflammatory disorders (e.g., such as allergy, asthma, leukemia, etc. and as described below under "Immune Activity", and "Blood-Related Disorders"). Highly preferred indications also includie
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.	Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or
	Production of IL-8 by by endothelial cells (such as Human Umbilical Cord Endothelial Cells).
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	HNGDJ72
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				secretion of IL-8. For	autoimmune disorders (e.g
				example. FMAT may be used	rheumatoid arthritis, systemic
				or routinely modified to assess	lupus erythematosis, Crohn"s
				the ability of polypeptides of	disease, multiple sclerosis
				the invention (including	and/or as described below),
				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
				vascular permeability, vascular	consequent complications
				tone, and immune cell	(such as acute respiratory
				extravasation. Endothelial	distress syndrome and
				cells play a pivotal role in the	systemic ischemia-reperfusion
				initiation and perpetuation of	resulting from septic shock),
				inflammation and secretion of	restnosis and atherosclerosis.
				IL-8 may play an important	
				role in recruitment and	
				activation of immune cells	
				such as neutrophils,	
·				macrophages, and	
		,		lymphocytes.	
1) 6	HNGDJ72	1313	Production of	RANTES FMAT. Assays for	
363			KAN1ES IN	immunomodulatory proteins	

cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical
endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	

	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and
approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular tone, and immune cell extravasation.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1313
	HNGDJ72
	365

inflammatory responses.	CD152 in Human T cells	Kinase assay. JNK kinase	Pathway assays for signal transduction include asthma, allergy,		activation, or apoptosis are inflammation, and		be used or routinely modified Additional highly preferred	to assess the ability of indications include immune	ention	(including antibodies and (e.g., as described below under	the	invention) to promote or "Blood-Related Disorders"),	inhibit cell proliferation, autoimmune diseases (e.g.,	activation, and apoptosis. rheumatoid arthritis, systemic	<u></u>	used or routinely modified to and/or as described below),	test JNK kinase-induced immunodeficiencies (e.g., as	activity of polypeptides of the described below). Highly	invention (including antibodies preferred indications also	and agonists or antagonists of include boosting or inhibiting	the invention) include the immune cell proliferation.	assays disclosed in Forrer et Preferred indications include	al., Biol Chem 379(8-9):1101- neoplastic diseases (e.g.,	1110 (1998); Gupta et al., Exp leukemia, lymphoma, and/or as	Cell Res 247(2): 495-504 described below under	(1999); Kyriakis JM, Biochem "Hyperproliferative	Soc Symp 64:29-48 (1999); Disorders"). Highly preferred	O. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.
	1314 CD152 in cells	1315 Activation of JNK	Signaling Pathway	in immune cells	(such as	eosinophils).																						
	HNGDU40	HNGE029														 												
	366		367						-					-		 			_									

eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.		
410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic	reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate	signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38

ts s	A preferred embodiment of the invention includes a method for inhibiting (e.g.	reducing) TNF alpha production. An alternative preferred embodiment of the
mitogen-activated protein kinase in human eosinophils". Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the Serum Response Element	(SRE) are well-known in the art and may be used or routinely modified to assess
	Activation of transcription through serum	response element in immune cells (such as T-cells).
	1316	
	HNGEP09	
	368	

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invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	
the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	
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									-								<u> </u>	- 137	-					•						

			Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	-		assays include the CTLL cell	under "Hyperproliferative
			line, which is an IL-2	Disorders"). Additionally,
	_		dependent suspension culture	highly preferred indications
			of T cells with cytotoxic	include neoplasms and
			activity.	cancers, such as, for example,
				leukemia, lymphoma,
				melanoma, glioma (e.g.,
				malignant glioma), solid
		10.4		tumors, and prostate, breast,
				lung, colon, pancreatic,
-				esophageal, stomach, brain,
				liver and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
-				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
-				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
	1			arthritis, AIDS, granulomatous
				disease, inflammatory bowel
<u>.</u>				disease, neutropenia,
				neutrophilia, psoriasis,

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		
		Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al.,
	HLA-DR in Human T cells	Inhibition of squalene synthetase gene transcription.
	1316	1317
	HNGEP09	HNGHR74
	368	369

nrotein (MCP), and the	"Immine Activity" "Blood-
activation of monocytes and T	
cells. Such assays that may be	
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
 polypeptides of the invention	
(including antibodies and	multiple sclerosis and/or as
 agonists or antagonists of the	
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	3- indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
reference in its entirety.	suppression of immune
 Human dendritic cells that may	ay reactions to transplanted
 be used according to these	organs and tissues,
assays may be isolated using	hemophilia, hypercoagulation,
techniques disclosed herein or	r diabetes mellitus, endocarditis,
otherwise known in the art.	meningitis (bacterial and
Human dendritic cells are	viral), Lyme Disease, asthma,
 antigen presenting cells in	and allergy Preferred
suspension culture, which,	indications also include

				when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
370	HNGIH43	1318	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmine diseases (e o
	regulate GATA3 transcription	rheumatoid arthritis. systemic
Mark Mark Mark Mark Mark Mark Mark Mark	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
-	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's

				contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used	lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,
				according to these assays are publicly available (e.g., through the ATCC).	neutrophilia, psoriasis, suppression of immune reactions to transplanted
·				Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
				immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	
				immature mast cells.	
370	HNGIH43	1318	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
			response element in	signating painway in FiMC-1 human mast cell line.	rninitis. Additional preferred indications include infection
			immune cells (such as mast cells).	Activation of NFAT in mast cells has been linked to	(e.g., an infectious disease as described below under
				cytokine and chemokine production. Assays for the	"Infectious Disease"), and inflammation and
				activation of transcription	inflammatory disorders.
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be used or routinely modified to	"Immune Activity", "Blood-Related Disorders" and/or
			1		TOTAL TOTAL STATE

"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred		dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's
assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-
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	-																													
																													•	•

				16338 (1995), and Turner et al. 1 Exp. Med 188:527-537	lymphoma, arthritis, AIDS, orannlomatous disease
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
		·		these assays include the HMC-	
				1 cell line, which is an	
		Š		immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
370	HNGIH43	1318	SEAP in UMR-106		
	HNGIJ31	1319	Activation of	Assays for the activation of	Preferred indications include
371			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
	-		-	agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred

indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	Inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma,	and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms	and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma,	Hodgkin"s disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other
and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of	cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test	cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are publicly available (e.g., through the ATCC).

			modified to assess the ability	inhibiting (e.g., reducing)
			of polypeptides of the	MCP-1 production. A highly
	*****		invention (including antibodies	is
			and agonists or antagonists of	infection (e.g., an infectious
			the invention) to mediate	disease as described below
J			immunomodulation, induce	under "Infectious Disease").
			chemotaxis, and modulate	Additional highly preferred
			immune cell activation.	indications include
			Exemplary assays that test for	inflammation and
			immunomodulatory proteins	inflammatory disorders.
			evaluate the production of cell	Preferred indications include
			surface markers, such as	blood disorders (e.g., as
			monocyte chemoattractant	described below under
			protein (MCP), and the	"Immune Activity", "Blood-
			activation of monocytes and T	Related Disorders", and/or
			cells. Such assays that may be	"Cardiovascular Disorders").
			used or routinely modified to	Highly preferred indications
			test immunomodulatory and	include autoimmune diseases
		***	diffferentiation activity of	(e.g., rheumatoid arthritis,
			polypeptides of the invention	systemic lupus erythematosis,
			(including antibodies and	multiple sclerosis and/or as
			agonists or antagonists of the	described below) and
			invention) include assays	immunodeficiencies (e.g., as
			disclosed in Miraglia et al., J	described below). Preferred
			Biomolecular Screening 4:193-	indications also include
		-	204(1999); Rowland et al.,	anemia, pancytopenia,
			"Lymphocytes: a practical	leukopenia, thrombocytopenia,
			approach" Chapter 6:138-160	Hodgkin's disease, acute
			(2000); Satthaporn and	lymphocytic anemia (ALL),
			Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
			45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,

				Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
				158:2919-2925 (1997), the	disease, inflammatory bowel
				contents of each of which are	disease, sepsis, neutropenia,
				herein incorporated by	neutrophilia, psoriasis,
				reference in its entirety.	suppression of immune
				Human dendritic cells that may	reactions to transplanted
				be used according to these	organs and tissues,
				assays may be isolated using	hemophilia, hypercoagulation,
				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
-				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
_				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
H	HNGIJ31	1319	Stimulation of	Assays for measuring secretion	A highly preferred

from pancreatic the art and may be used or beta cells. the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, 138(9):3735-40 (1997); Kim,	371	insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim,	7.7	from monorous	the out and may be used or	An additional highly preferred
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim,		Iroin pancicane	ule all alla lilay of used of	indication is a complication
of a lin, et l		beta cells.	routinely modified to assess	Illuication is a compilication
tion ng d d d d d d d d d d d d d d d d d d			the ability of polypeptides of	associated with diabetes (e.g.,
tion ng d d d d d d d d d d d d d d d d d d			the invention (including	diabetic retinopathy, diabetic
tion ng d d d d d d d d d d d d d d d d d d			antibodies and agonists or	nephropathy, kidney disease
on on in			antagonists of the invention) to	(e.g., renal failure,
g g g g g g g g g g g g g g g g g g g			stimulate insulin secretion.	nephropathy and/or other
g g for to to dies of dies m, m,			For example, insulin secretion	diseases and disorders as
to t			is measured by FMAT using	described in the "Renal
be to the in the state of the et the			anti-rat insulin antibodies.	Disorders" section below),
to be e e e e e e e e e e e e e e e e e e			Insulin secretion from	diabetic neuropathy, nerve
to to in in dies of dies of m,			pancreatic beta cells is	disease and nerve damage
to to to of dies of m,			upregulated by glucose and	(e.g., due to diabetic
it may be lifted to insulin eatic of the ntibodies onists of assays b., et al., ot i, M., et li, M., et li, Kim,			also by certain	neuropathy), blood vessel
s. t may be liftied to insulin eatic s of the antibodies onists of a sasays 3, et al., Pt i, M., et			proteins/peptides, and	blockage, heart disease, stroke,
t may be liftied to insulin eatic s of the antibodies onists of assays 3., et al., Pt i, M., et			disregulation is a key	impotence (e.g., due to diabetic
0 0 0			component in diabetes.	neuropathy or blood vessel
S (1			Exemplary assays that may be	blockage), seizures, mental
if if			used or routinely modified to	confusion, drowsiness,
it if the			test for stimulation of insulin	nonketotic hyperglycemic-
if the state of th			secretion (from pancreatic	hyperosmolar coma,
if if			cells) by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
			disclosed in: Ahren, B., et al.,	diseases and disorders as
			Am J Physiol, 277(4 Pt	described in the
			2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
-			al., Endocrinology,	section below), dyslipidemia,
			138(9):3735-40 (1997); Kim,	endocrine disorders (as

			K.H., et al., FEBS Lett,	described in the "Endocrine
			377(2):237-9 (1995); and,	Disorders" section below),
			Miraglia S et. al., Journal of	neuropathy, vision impairment
			Biomolecular Screening,	(e.g., diabetic retinopathy and
			4:193-204 (1999), the contents	blindness), ulcers and impaired
			of each of which is herein	wound healing, and infection
			incorporated by reference in its	(e.g., infectious diseases and
			entirety. Pancreatic cells that	disorders as described in the
			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
			used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	r alterna
			rat transplantable insulinoma.	weight gain. Aditional
.			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
		•	secretion. References: Asfari	
			et al. Endocrinology 1992	
			130:167.	
HNGIJ31	1319	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
		PI3 Kinase	assay, for PI3 kinase signal	includes a method for
		Signalling Pathway	transduction that regulate	increasing muscle cell survival

An alternative highly preferred embodiment of the invention	includes a method for	decreasing muscle cell	survival. A preferred	embodiment of the invention	includes a method for	stimulating muscle cell	proliferation. In a specific	embodiment, skeletal muscle	cell proliferation is stimulated.	An alternative highly preferred	embodiment of the invention	includes a method for	inhibiting muscle cell	proliferation. In a specific	embodiment, skeletal muscle	cell proliferation is inhibited.	A preferred embodiment of	the invention includes a	method for stimulating muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	stimulated. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is
glucose metabolism and cell survivial are well-known in the		ssess		the invention (including	or	n) to		'al.		e	used or routinely modified to	ţ	of polypeptides of the	ntibodies			loi	Chem 379(8-9):1101-1110		Diabetes 49(2):263-271	(2000); and Schreyer et al.,	_	l of		by reference in its entirety.	Rat myoblast cells that may be		are publicly available (e.g.,	through the ATCC).
	-																					•				-			
			3.5												-														
		_																						-					

cells inhibited. Highly preferred ag indications include disorders of the musculoskeletal system. Preferred indications include		<u></u>	Disorders"), neural disorders (e.g., as described below under	"Neural Activity and Neurological Diseases"), blood	disorders (e.g., as described below under "Immune	Activity", "Cardiovascular Disorders", and/or "Blood-	Related Disorders"), immune disorders (e.g., as described	below under "Immune Activity"), and infection (e.g.,	as described below under "Infectious Disease").	highly preferred indication is	diabetes mellitus. An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic
Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast	cell line, isolated from primary cultures of rat thigh muscle, that fuses to form	multinucleated myotubes and striated fibers after culture in differentiation media.												

(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are	complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system including myopathies,	muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart	fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and

vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	7 %
	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
	1320
	HNGIQ46
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used or routinely modified to	and/or as described below).
test JNK kinase-induced	immunodeficiencies (e.g., as
activity of polypeptides of the	described below). Highly
invention (including antibodies	preferred indications also
and agonists or antagonists of	include boosting or inhibiting
the invention) include the	immune cell proliferation.
assays disclosed in Forrer et	Preferred indications include
al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
Cell Res 247(2): 495-504	described below under
(1999); Kyriakis JM, Biochem	"Hyperproliferative
Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
 Chang and Karin, Nature	indications include boosting an
410(6824):37-40 (2001); and	eosinophil-mediated immune
Cobb MH, Prog Biophys Mol	response, and suppressing an
Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
the contents of each of which	response.
are herein incorporated by	
reference in its entirety.	
Exemplary cells that may be	
used according to these assays	
include eosinophils.	
Eosinophils are important in	
the late stage of allergic	
reactions; they are recruited to	
tissues and mediate the	
inflammatory response of late	
stage allergic reaction.	
Moreover, exemplary assays	
that may be used or routinely	
modified to assess the ability	

of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-
							- 410				-																		

				terminal kinase	
				phosphorylation" J Allergy	
				Clin Immunol; Sep;104(3 Pt	
				1):565-74 (1999); the contents	
				of each of which are herein	
				incorporated by reference in its	
				entirety.	
	HNGJE50	1321	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
373				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
	-			disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
			-	expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
		,		used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
			1 to	polypeptides of the invention	rheumatoid arthritis, systemic

(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
may be used or routinely	disorders.Additional highly
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative
204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lymphocytes: a practical	indications include neoplasms
 approach" Chapter 6:138-160	and cancers, such as, myeloma,
(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
(1997), the contents of each of	prostate, breast, lung, colon,
which are herein incorporated	pancreatic, esophageal,

				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
		-		antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
	44.00			and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
			7.2.4		reactions to transplanted
		A-84			organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HNGJE50	1321	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
373				of insulin are well-known in	is diabetes mellitus. An

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additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal Disorders" section below),	discase and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic	blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis,	hypertension, stroke, and other	diseases and disorders as described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine
the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to stimulate insulin secretion.	For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.	Insulin secretion from pancreatic beta cells is unregulated by glucose and	also by certain proteins/peptides, and	disregulation is a key	Exemplary assays that may be	used or routinely modified to test for stimulation of insulin	secretion (from pancreatic cells) by polypeptides of the	invention (including antibodies	the invention) include assays	disclosed in: Shimizu, H., et	(2000); Salapatek, A.M., et al.,	Mol Endocrinol, 13(8):1305-	17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4
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		A Company	(1998): Olson. L.K et al J	Disorders" section below).
-			Biol Chem, 271(28):16544-52	neuropathy, vision impairment
			(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
			Journal of Biomolecular	blindness), ulcers and impaired
			Screening, 4:193-204 (1999),	wound healing, and infection
			the contents of each of which	(e.g., infectious diseases and
			is herein incorporated by	disorders as described in the
			reference in its entirety.	"Infectious Diseases" section
			Pancreatic cells that may be	below, especially of the
			used according to these assays	urinary tract and skin), carpal
			are publicly available (e.g.,	tunnel syndrome and
			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
	-		transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
		0	somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
			cells secrete insulin, which is	
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
	40-100-400-40		glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	

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					A highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	TNF alpha production. An	alternative highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple
Natl. Acad. Sci. USA 78: 4339-4343, 1981.					TNFa FMAT. Assays for	immunomodulatory proteins	produced by activated	macrophages, T cells,	fibroblasts, smooth muscle,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of
	IgG in Human B cells SAC	TNFa in Human T-cell 293T	IL-10 in Human T-cell 2B9	CXCR4 in SW480	Production of TNF	alpha by dendritic	cells																		
	1321	1321	1321	1321	1322																				
	HNGJE50	HNGJE50	HNGJE50	HNGJE50	HNGJO57																				
	373	373	373	373		374				224															

sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications	include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such	assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J	Immunol 100(7):3383-3393 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using

				techniques disclosed herein or	disorders and pre-neoplastic
	_			otherwise known in the art.	conditions, such as, for
				Human dendritic cells are	example, hyperplasia,
				antigen presenting cells in	metaplasia, and/or dysplasia.
				suspension culture, which,	Preferred indications include
				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
		•		upregulate T cell proliferation	Hodgkin's disease, acute
-				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
			450-4		diabetes mellitus, endocarditis,
			-		meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
374	HNGJ057	1322	IFNg in Human T-cell 293T		
	HNGJP69	1323	SEAP in 293/ISRE	and the second s	
375		į			

	HNGJP69	1323	Activation of	Assays for the activation of	A highly preferred indication
375			transcription	transcription through the	is obesity and/or complications
		772.73	through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
· -		_		polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
		**************************************		invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
		-		signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
-				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
		_		transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,
				modified to test cAMP-	heart disease, atherosclerosis,

response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	Je	r A r	Klemm et al., J Biol Chem (e.g., infectious diseases and 273:917-923 (1998), the contents of each of which are herein incorporated by below, especially of the	adipocytes that may be used according to these assays are publicly available (e.g., publicly available (e.g., publicly and/or publications are complications	2	include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3
response element activity polypeptides of the inven (including antibodies and agonists or antagonists of	invention) include assays disclosed in Berger et al., 66:1-10 (1998); Cullen ar Malm, Methods in Enzyn	216:362-368 (1992) et al., Proc Natl Aca 85:6342-6346 (1988 et al., Mol Cell Biol	Klemm et al., J Biol Che 273:917-923 (1998), the contents of each of which herein incorporated by	reference in its entirety. adipocytes that may be according to these assay publicly available (e.g., through the ATCC) and	may be routinely generate Exemplary mouse adipoc cells that may be used according to these assays	include 3T3-L1 cells. 3T is an adherent mouse preadipocyte cell line that continuous substrain of 3T

				through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
375	HNGJP69	1323	Activation of transcription through serum response element in pre-adipocytes.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992): Henthorn et al	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, hood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental

				Proc Natl Acad Sci USA	confusion, drowsiness,
				85:6342-6346 (1988); and	nonketotic hyperglycemic-
				Black et al., Virus Genes	hyperosmolar coma,
				12(2):105-117 (1997), the	cardiovascular disease (e.g.,
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
				reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
			-	Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
		,		conditions known in the art.	insulin resistance.
	HNGJP69	1323	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
375			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred

indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"),	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as	preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative".	Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.
to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or	inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils.

Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J
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	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammation and include blood disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic	sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred	indications include neoplastic diseases (e.g., leukemia,	lymphoma, melanoma, prostate, breast, lung, colon.	pancreatic, esophageal,	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliterative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,		leukemias, Hodgkin's disease,		(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,
antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription	expression of mast cell genes important for immune response	development. Exemplary assays for transcription	through the GATA3 response element that may be used or	routinely modified to test GATA3-response element	activity of polypeptides of the	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are
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granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
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	HNGJP69
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Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et
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granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under
al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the
	Activation of transcription through NFKB response element in immune cells (such as basophils).
	1323
	HNGJP69
	375

"Immune Activity", and	"Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".				
invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used

				according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	
375	HNGJP69	1323	SEAP in Ku812/NFkB (TNF synergy)		
376	HNGJT54	1324	Activation of	Assays for the activation of	Preferred indications include
0/6			through cAMP	campoint unough the campoint are	described below under
		71.4	response element in	well-known in the art and may	"Immune Activity", "Blood-
			as T-cells).	be used or rounnely modified to assess the ability of	Related Disorders', and/or "Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	•
				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
•••				transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
		···		cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
				through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated

			activity of nolyneptides of the	immune response. Additional
			invention (including antibodies	nreferred indications include
			and acquiete or antagonists of	inflammation and
			and agonists of antagonists of	Commence discourt description
			the invention) include assays	inflammatory disorders.
-			disclosed in Berger et al., Gene	Highly preferred indications
			66:1-10 (1998); Cullen and	include neoplastic diseases
			Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
			216:362-368 (1992); Henthorn	and/or as described below
			et al., Proc Natl Acad Sci USA	under "Hyperproliferative
			85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Genes 15(2):105-117	indications include neoplasms
			(1997); and Belkowski et al., J	and cancers, such as, for
			Immunol 161(2):659-665	example, leukemia, lymphoma
			(1998), the contents of each of	(e.g., T cell lymphoma,
			which are herein incorporated	Burkitt's lymphoma, non-
			by reference in its entirety. T	Hodgkins lymphoma,
			cells that may be used	Hodgkin"s disease),
			according to these assays are	melanoma, and prostate,
			publicly available (e.g.,	breast, lung, colon, pancreatic,
			through the ATCC).	esophageal, stomach, brain,
-			Exemplary mouse T cells that	liver and urinary cancer. Other
	-		may be used according to these	preferred indications include
•			assays include the CTLL cell	benign dysproliferative
			line, which is a suspension	disorders and pre-neoplastic
			culture of IL-2 dependent	conditions, such as, for
			cytotoxic T cells.	example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
- "				anemia, pancytopenia,
-				leukopenia, thrombocytopenia,
				acute lymphocytic anemia

(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of
	Activation of transcription through serum response element in immune cells (such as T-cells).
·	1324
	HNGJT54
	376

	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
 	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
 	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
-		leukemia, lymphoma,
		melanoma, glioma (e.g.,
 		malignant glioma), solid
 		tumors, and prostate, breast,
		lung, colon, pancreatic,

			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			 benign dysproliferative
			disorders and pre-neoplastic
-			conditions, such as, for
_			example, hyperplasia,
-			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			 leukopenia, thrombocytopenia,
	-	-	Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			 arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			 disease, neutropenia,
			 neutrophilia, psoriasis,
			 suppression of immune
			 reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			 diabetes mellitus, endocarditis,
			 meningitis, Lyme Disease,
			 cardiac reperfusion injury, and
			asthma and allergy. An
			additional preferred indication
			 is infection (e.g., an infectious
			disease as described below
			under "Infectious Disease").

	HNGIT54	1324	Production of	MCP-1 FMAT. Assays for	A highly preferred
376		1	MCP-1	immunomodulatory proteins	embodiment of the invention
)				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
	- 12			activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for
				modified to assess the ability	inhibiting (e.g., reducing)
				of polypeptides of the	MCP-1 production. A highly
				invention (including antibodies	preferred indication is
				and agonists or antagonists of	infection (e.g., an infectious
				the invention) to mediate	disease as described below
				immunomodulation, induce	under "Infectious Disease").
				chemotaxis, and modulate	Additional highly preferred
				immune cell activation.	indications include
	_			Exemplary assays that test for	inflammation and
				immunomodulatory proteins	inflammatory disorders.
				evaluate the production of cell	Preferred indications include
				surface markers, such as	blood disorders (e.g., as
				monocyte chemoattractant	described below under
				protein (MCP), and the	"Immune Activity", "Blood-
				activation of monocytes and T	Related Disorders", and/or
				cells. Such assays that may be	"Cardiovascular Disorders").
				used or routinely modified to	Highly preferred indications
				test immunomodulatory and	include autoimmune diseases
				diffferentiation activity of	(e.g., rheumatoid arthritis,
				polypeptides of the invention	systemic lupus erythematosis,
 -				(including antibodies and	multiple sclerosis and/or as
-				agonists or antagonists of the	described below) and
				invention) include assays	immunodeficiencies (e.g., as

disclosed in Miraglia et al., J	disclosed in Miraglia et al., J	described below). Preferred
204(1999); Rowland et al.,	creening 4:193- vland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	oter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	orn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	ll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	1); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	(1997), the	disease, inflammatory bowel
contents of each of which are	n of which are	disease, sepsis, neutropenia,
herein incorporated by	ated by	neutrophilia, psoriasis,
reference in its entirety.	entirety.	suppression of immune
Human dendrii	Human dendritic cells that may	reactions to transplanted
be used according to these	ng to these	organs and tissues,
assays may be isolated using	solated using	hemophilia, hypercoagulation,
techniques disk	techniques disclosed herein or	diabetes mellitus, endocarditis,
otherwise known in the art.	n in the art.	meningitis (bacterial and
Human dendritic cells are	c cells are	viral), Lyme Disease, asthma,
antigen presenting cells in	ng cells in	and allergy Preferred
suspension culture, which,	ure, which,	indications also include
when activated by antigen	by antigen	neoplastic diseases (e.g.,
and/or cytokines, initiate and	s, initiate and	leukemia, lymphoma, and/or as
upregulate T cell proliferation	ll proliferation	described below under
and functional activities.	ctivities.	"Hyperproliferative
		Disorders"). Highly preferred
		indications include neoplasms
		and cancers, such as, leukemia,
		lymphoma, prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,

2267	HNGKN89	325	Activation of transcription through cAMP response element (CRE) in preadipocytes.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
				functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors	nephropathy and/or other diseases and disorders as described in the "Renal
				that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the	Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,

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neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuronathy vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal	tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.
transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that	may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci 11SA	85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-	adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte

		Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"), and/or "Cardiovascular Disorders").
cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.		This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
	SEAP in HIB/CRE	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	1325	1325
	HNGKN89	HNGKN89
	377	377

rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred indications include neoplastic	diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary tract cancers and/or as	described below under "Hyperproliferative	Disorders"). Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions. Such	as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease, acute lymphocytic anemia		lymphoma, arthritis, AIDS,	granulomatous disease, inflammatory howel disease
regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response	development. Exemplary assays for transcription through the GATA3 response	element that may be used or routinely modified to test GATA3-response element	activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm. Methods in Enzymol	216:362-368 (1992); Henthorn	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924	(1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	contents of each of which are	herein incorporated by
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				cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
377	HNGKN89	1325	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention fincluding antibodies and	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include

	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lumis erythematosis multiple
	invention) to legarate 141 Ast	iupus ei y mempis, mumpis
	transcription factors and	scierosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,

ety. ety. used ys are reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, ding to meningitis, and Lyme Disease. e HMC- e HMC- mast mast lbits f	he the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune ate the Activity", "Blood-Related ated
which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the activation of transcription through the Serum Response Element in (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1326
	HNGOM56
	378

	genes in many cell types	"Cardiovascular Disorders")
	Exemplary assays for	Highly preferred indications
	transcription through the SRE	include autoimmune diseases
	that may be used or routinely	(e a rheumatoid arthritis
	modified to test SRF activity	evetemic lunus erythematosis
	of the polynentides of the	Cropp"s disease multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below), immunodeficiencies
 	the invention) include assays	(e.g., as described below),
	disclosed in Berger et al., Gene	boosting a T cell-mediated
	66:1-10 (1998); Cullen and	immune response, and
	Malm, Methods in Enzymol	suppressing a T cell-mediated
	216:362-368 (1992); Henthorn	immune response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
-	85:6342-6346 (1988); Benson	include inflammation and
	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
 	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.
-	by reference in its entirety.	Highly preferred indications
	Human T cells that may be	include neoplastic diseases
	used according to these assays	(e.g., leukemia, lymphoma,
	are publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
	Exemplary human T cells that	Disorders"). Additionally,
	may be used according to these	highly preferred indications
-	assays include the JURKAT	include neoplasms and
	cell line, which is a suspension	cancers, such as, leukemia,
	culture of leukemia cells that	lymphoma, melanoma, glioma
	produce IL-2 when stimulated.	(e.g., malignant glioma), solid

		tumors, and prostate, breast, lung, colon, pancreatic,
	•	esophageal, stomach, brain,
		liver and urinary cancer. Other
	-	benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
-		cardiac reperfusion injury, and
		asthma and allergy. An
****		additional preferred indication
		is infection (e.g., an infectious

disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method		growth. A highly preferred	embodiment of the invention	includes a method for	stimulating anontosis of
	Caspase Apoptosis Rescue. Assays for caspase apoptosis	rescue are well known in the art and may be used or	routinely modified to assess	the ability of the polypeptides	antibodies and agonists or	antagonists of the invention) to	inhibit caspase protease-	mediated apoptosis.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	caspase apoptosis rescue of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Romeo et al.,	Cardiovasc Res 45(3): 788-794	(2000); Messmer et al., Br J	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be
	Protection from Endothelial Cell	Apoptosis.																								
	1327		·																							
	HNGOU56																									
	379																									

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endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,
used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.															202	
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cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to the total control

sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atheroselerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Revnaud"s
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		٦	/prevention of endometriosis
			and related conditions.
			Additional highly preferred
			indications include fibromas,
			heart disease, cardiac arrest,
			heart valve disease, and
			vascular disease. Preferred
			indications include blood
			disorders (e.g., as described
			below under "Immune
			Activity", "Blood-Related
			Disorders", and/or
			"Cardiovascular Disorders").
			Preferred indications include
			autoimmune diseases (e.g.,
			rheumatoid arthritis, systemic
			lupus erythematosis, multiple
			sclerosis and/or as described
			below) and
			immunodeficiencies (e.g., as
			described below). Additional
			preferred indications include
			inflammation and
			inflammatory disorders (such
			as acute and chronic
			inflammatory diseases, e.g.,
			inflammatory bowel disease
			and Crohn's disease), and pain
	7 Y Y W W. W		management.
 HNGOU56	1327	IL-10 in Human T-	
		2001	

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	Thromb 3(2); 75-80 (1996);	for inhibiting endothelial cell
	the contents of each of which	growth. A highly preferred
	are herein incorporated by	ent
	reference in its entirety.	includes a method for
	Endothelial cells that may be	stimulating apoptosis of
	used according to these assays	endothelial cells. An
	are publicly available (e.g.,	alternative highly preferred
	through commercial sources).	embodiment of the invention
	Exemplary endothelial cells	includes a method for
	that may be used according to	inhibiting (e.g., decreasing)
-	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	A highly preferred
	(bAEC), which are an example	embodiment of the invention
	of endothelial cells which line	includes a method for
	blood vessels and are involved	stimulating angiogenisis. An
	in functions that include, but	alternative highly preferred
	are not limited to,	embodiment of the invention
	angiogenesis, vascular	includes a method for
	permeability, vascular tone,	inhibiting angiogenesis. A
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for reducing cardiac
		hypertrophy. An alternative
		highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
-		described below under
		"Hyperproliferative

	Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or
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cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors,	reukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary	angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,

such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic
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					-																						-			

and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,
						-										-														
														- 18							-							-		

					inflammatory bowel disease
					and Crohn's disease), and pain management.
380	HNGOW62	1328	IL-10 in Human T-cell 293T		
380	HNGOW62	1328	TNFa in Human T-cell 293T		
100	HNHAH01	1329	Activation or	This reporter assay measures	
381			inhibition of transcription	activation or inhibition of the NFkB signaling pathway in	
•			through NFKB	Ku812 human basophil cell	
			response element in	line. Assays for the activation	
			immune cells (such	or inhibition of transcription	
			as basophils).	through the NFKB response	
				element are well-known in the	
				art and may be used or	
				routinely modified to assess	
				the ability of polypeptides of	
				the invention (including	
				antibodies and agonists or	
		-2-1		antagonists of the invention) to	
				regulate NFKB transcription	
				factors and modulate	
				expression of	
				immunomodulatory genes.	
				NFkB is important in the	
				pathogenesis of asthma.	
				Exemplary assays for	
				transcription through the	
	101			NFKB response element that	
				may be used or rountinely	

modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone et al, Int Arch Allergy Immunol 114(3):207-17	(1997), the contents of each of which are herein incorporated	Cells were pretreated with SID supernatants or controls for 15-	of TNF was added to stimulate the NFkB reporter. SEAP activity was measured after 48	hours. Basophils that may be used according to these assays	are publicly available (e.g., through the ATCC). Exemplary human basophil	cell lines that may be used according to these assays include Ku812, originally
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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein
	Production of ICAM-1
	1329
	HNHAH01
	86 2390

	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage
incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in
	Activation of transcription through cAMP response element (CRE) in preadipocytes.
	1330
	HNHCX60
	382

		in differentiation into	neuronathy), blood vessel
	8	adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
	I	Exemplary assays for	confusion, drowsiness,
	t	transcription through the	nonketotic hyperglycemic-
	5	cAMP response element that	hyperosmolar coma,
	1	may be used or routinely	cardiovascular disease (e.g.,
	1	modified to test cAMP-	heart disease, atherosclerosis,
		response element activity of	microvascular disease,
-		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
		agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
		Malm, Methods in Enzymol	described in the "Endocrine
		216:362-368 (1992); Henthorn	Disorders" section below),
	9	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	9	et al., Mol Cell Biol	blindness), ulcers and impaired
		20(3):1008-1020 (2000); and	wound healing, and infection
		Klemm et al., J Biol Chem	(e.g., infectious diseases and
		273:917-923 (1998), the	disorders as described in the
		contents of each of which are	"Infectious Diseases" section
		herein incorporated by	below, especially of the
	ı	reference in its entirety. Pre-	urinary tract and skin), carpal
-		adipocytes that may be used	tunnel syndrome and
	-	according to these assays are	Dupuytren's contracture).
		publicly available (e.g.,	Additional highly preferred

indications are complications associated with insulin resistance.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	1330
	HNHCX60
	382

		polypeptides of the invention	lupus erythematosis, multiple
		(including antibodies and	sclerosis and/or as described
		agonists or antagonists of the	below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
	*	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver, and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary mouse T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the CTLL cell	example, hyperplasia,
		line, which is an IL-2	metaplasia, and/or dysplasia.
		dependent suspension-culture	Preferred indications include
		cell line with cytotoxic	arthritis, asthma, AIDS,
		activity.	allergy, anemia, pancytopenia,
			leukopenia, thrombocytopenia,

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus
	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Production of IFNgamma using a T cells
	1331
	HNHCY64
	383

osteoporosis, and/or as described below under "Infectious Disease") Hiohly	preferred indications include	autoimmune disease (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,
(including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation, regulate	minammatory activities, modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad	Sci 856;22-32 (1998); Boehm
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		÷																-	-								
												-															

				et al., Annu Rev Immunol	breast, lung, colon, pancreatic.
				15:749-795 (1997), and	esophageal, stomach, brain,
				Rheumatology (Oxford)	liver and urinary cancer. Other
				38(3):214-20 (1999), the	preferred indications include
				contents of each of which are	benign dysproliferative
-				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
		-		Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
-				techniques disclosed herein or	anemia, pancytopenia,
		*		otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
		186		human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HNHCY94	1332	Activation of	Assays for the activation of	Preferred indications
384			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative

		immune cells (such	routinely modified to assess	Disorders"), blood disorders
		as T-cells).	the ability of polypeptides of	(e.g., as described below under
			the invention (including	"Immune Activity",
			antibodies and agonists or	"Cardiovascular Disorders",
			antagonists of the invention) to	and/or "Blood-Related
			modulate growth and other cell	Disorders"), and infection
-			functions. Exemplary assays	(e.g., an infectious disease as
			for transcription through the	described below under
			AP1 response element that	"Infectious Disease"). Highly
			may be used or routinely	preferred indications include
			modified to test AP1-response	autoimmune diseases (e.g.,
			element activity of	rheumatoid arthritis, systemic
			polypeptides of the invention	lupus erythematosis, multiple
			(including antibodies and	sclerosis and/or as described
			agonists or antagonists of the	below) and
			invention) include assays	immunodeficiencies (e.g., as
			disclosed in Berger et al., Gene	described below). Additional
	•		66:1-10 (1988); Cullen and	highly preferred indications
			Malm, Methods in Enzymol	include inflammation and
-		•	216:362-368 (1992); Henthorn	inflammatory disorders.
			et al., Proc Natl Acad Sci USA	Highly preferred indications
			85:6342-6346 (1988);	also include neoplastic
			Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
			272(49):30806-30811 (1997);	lymphoma, and/or as described
	-		Chang et al., Mol Cell Biol	below under
	_		18(9):4986-4993 (1998); and	"Hyperproliferative
			Fraser et al., Eur J Immunol	Disorders"). Highly preferred
			29(3):838-844 (1999), the	indications include neoplasms
	_		contents of each of which are	and cancers, such as, leukemia,
			herein incorporated by	lymphoma, prostate, breast,
			reference in its entirety. T	lung, colon, pancreatic,

				cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, endocarditis, meningitis, and I vme Disease.
NH I	HNHDW38	1333	CD71 in Human T cells		
E C	HNHDW42	1334	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6	A highly preferred embodiment of the invention includes a method for
				participates in IL-4 induced IgE production and increases IgA production (IgA plays a	stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment

	role in m	role in mucosal immunity).	of the invention includes a
	IL-6 indt	IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
	Deregula	Deregulated expression of IL-6	reducing) IL-6 production. A
	has been	has been linked to autoimmune	highly preferrred indication is
	disease, 1	disease, plasmacytomas,	the stimulation or enhancement
	myeloma	myelomas, and chronic	of mucosal immunity. Highly
	hyperpro	hyperproliferative diseases.	preferred indications include
	Assays fo	Assays for immunomodulatory	blood disorders (e.g., as
	and diffe	and differentiation factor	described below under
	proteins	proteins produced by a large	"Immune Activity", "Blood-
	variety o	variety of cells where the	Related Disorders", and/or
	expressic	expression level is strongly	"Cardiovascular Disorders"),
	regulated	regulated by cytokines, growth	and infection (e.g., as
	factors, a	factors, and hormones are well	described below under
	known ir	known in the art and may be	"Infectious Disease"). Highly
	nsed or r	used or routinely modified to	preferred indications include
	assess the	assess the ability of	autoimmune diseases (e.g.,
	polypepti	polypeptides of the invention	rheumatoid arthritis, systemic
	(includin	(including antibodies and	lupus erythematosis, multiple
	agonists	agonists or antagonists of the	sclerosis and/or as described
	invention	invention) to mediate	below) and
	immunor	immunomodulation and	immunodeficiencies (e.g., as
	differenti	differentiation and modulate T	described below). Highly
	cell proli	cell proliferation and function.	preferred indications also
	Exempla	Exemplary assays that test for	include boosting a B cell-
	immunor	immunomodulatory proteins	mediated immune response
	evaluate	evaluate the production of	and alternatively suppressing a
	cytokines	cytokines, such as IL-6, and	B cell-mediated immune
-	the stimu		response. Highly preferred
	upregulat	upregulation of T cell	indications include
	proliferat	proliferation and functional	inflammation and

		activities. Such assays that	inflammatory
		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
. .		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
	,	by reference in its entirety.	stomach, brain, liver and
_		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
	-	Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,
		and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's

				inflammatory bowel disease, sensis neutronenia
				sepsis, neutropeina, neutrophilia, psoriasis,
				reactions to transplanted
				organs and tissues,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
	•,			indication is infection (e.g., an
	-			infectious disease as described
				below under "Infectious
HNHDW42	1334	CD69 in Human T		Disease).
386		cells		
HNHDW42	1334	Hexosaminidase in		
		KBL-2H3		
HNHED17	1335	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
387			by T cells and has strong	embodiment of the invention
			effects on B cells. IL-6	includes a method for
	•		participates in IL-4 induced	stimulating (e.g., increasing)
			IgE production and increases	IL-6 production. An alternative
			IgA production (IgA plays a	highly preferred embodiment
			role in mucosal immunity).	of the invention includes a
			IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
			Deregulated expression of IL-6	reducing) IL-6 production. A
			has been linked to autoimmune	highly preferrred indication is
			disease, plasmacytomas,	the stimulation or enhancement

		myelomas, and chronic	of mucosal imminity Highly
-		hyperproliferative diseases.	preferred indications include
		Assays for immunomodulatory	blood disorders (e.g., as
 		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
 		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
•		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
180		assess the ability of	autoimmune diseases (e.g.,
		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
 - 1		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
 	-	activities. Such assays that	inflammatory
-		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include

	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
-	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
•	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
-	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,

388	HNHE142 HNHE142	1336	SEAP in HIB/CRE Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage.	suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred infication is infectious below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF.
				macropnage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory	righly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., as described below under "Infectious Disease". Highly preferred indications include blood disorders (e.g.,

		proteins that promote the	neutropenia (and the
		production of GM-CSF are	prevention of neutropenia
		well known in the art and may	(e.g., in HIV infected patients),
		be used or routinely modified	and/or as described below
		to assess the ability of	under "Immune Activity",
		polypeptides of the invention	"Blood-Related Disorders",
		(including antibodies and	and/or "Cardiovascular
		agonists or antagonists of the	Disorders"). Highly preferred
		invention) to mediate	indications also include
		immunomodulation and	autoimmune diseases (e.g.,
		modulate the growth and	rheumatoid arthritis, systemic
		differentiation of leukocytes.	lupus erythematosis, multiple
	-	Exemplary assays that test for	sclerosis and/or as described
		immunomodulatory proteins	below) and
		evaluate the production of	immunodeficiencies (e.g., as
		cytokines, such as GM-CSF,	described below). Additional
		and the activation of T cells.	highly preferred indications
-		Such assays that may be used	include asthma. Highly
		or routinely modified to test	preferred indications include
		immunomodulatory activity of	neoplastic diseases (e.g.,
	-	polypeptides of the invention	leukemia (e.g., acute
		(including antibodies and	lymphoblastic leukemia, and
		agonists or antagonists of the	acute myelogenous leukemia),
		invention) include the assays	lymphoma (e.g., non-
		disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
		Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
		204 (1999); Rowland et al.,	described below under
	-	"Lymphocytes: a practical	"Hyperproliferative
		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); and Ye et al., J Leukoc	indications include neoplasms
		Biol (58(2):225-233, the	and cancers, such as, leukemia,

	contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques	lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
	disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc	as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications include: suppression of immune reactions to transplanted organs and tissues (e.g., bone marrow transplant); accelerating myeloid recovery; and mobilizing hematopoietic progenitor cells. Preferred
,	receptors, leading to cell-mediated cytotoxicity.	T cell-mediated immune response, and alternatively, suppressing a T cell-mediated immune response. Preferred immune response. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel

disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.																						
			Kinase assay: measures the	phosphorylation of Elk-1, an indication of activation of	extracellular signal regulated	kinase (ERK). ERK pathway	regulates cell growth,	proliferation and	differentiation. Cells were	pretreated with SID	supernatants for 15-18 hours,	and then 100 nM of insulin	was added to stimulate ERK	kinase. Phosphorylation of	Elk-1 was measured after a 20	minute incubation. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte
	SEAP in HIB/CRE	IL-2 in Human T- cell 2B9	Inhibition of	adipocyte EKK signaling pathway.																		
	1337	1337	1338																			
	HNHF029	HNHF029	HNHFR04					-														
	389	389	390																			

cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiated to an adipose-like state before being used in the screen. See Green et al., Cell 3: 127-133 (1974), the contents of which are herein incorporated by reference in its entirety. HNHFR04 1338 Activation of Assays for the activation of transcription through the through NFKB NFKB response element are response element in immune cells (such be used or routinely modified as EOL1 cells). pulypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and
HNHFR04

"Immune Activity", and "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g.,	lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as	described below).				
immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that	may be used of foundiery modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle	Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of	which are herein incorporated by reference in its entirety. For example, a reporter assay (which measures increases in transcription inducible from a	NFkB responsive element in EOL-1 cells) may link the NFKB element to a repeorter

		A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific
gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.		Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose
	SEAP in HIB/CRE	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway
	1338	1338
	HNHFR04	HNHFR04
	390	390

metabolism and cell survival.
Exemplary assays for PI3
kinase activity that may be
used or routinely modified to
test PI3 kinase-induced activity
of polypeptides of the
invention (including antibodies
and agonists or antagonists of
the invention) include assays
disclosed in Forrer et al., Biol
Chem 379(8-9):1101-1110
(1998); Nikoulina et al.,
Diabetes 49(2):263-271
(2000); and Schreyer et al.,
Diabetes 48(8):1662-1666
(1999), the contents of each of
which are herein incorporated
by reference in its entirety.
Rat myoblast cells that may be
used according to these assays
are publicly available (e.g.,
through the ATCC).
Exemplary rat myoblast cells
that may be used according to
these assays include L6 cells.
L6 is an adherent rat myoblast
cell line, isolated from primary
cultures of rat thigh muscle,
that fuses to form
multinucleated myotubes and
striated fibers after culture in

below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	Neurological Diseases") blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage heart
differentiation media.																					•								
										-																			

complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly	preferred indications include	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,
						-																								
																					-						-			
														-																

					and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
390	HNHFR04	1338	Activation of transcription through NFKB response element in neuronal cells (such as SKNMC cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of neuronal genes. Exemplary	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer"s Disease, Parkinson"s Disease, Brain Cancer, Seizures).
				assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis, 7(4):448-461	

	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
(2000); Tamatani M, et al., J Biol Chem, 274(13):8531-8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
	1339
	HNHFU32
	391

and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred	e ii.	lupus erythematosis, multiple sclerosis and/or as described	(e.g., as described below), boosting a T cell-mediated	immune response, and	immune response. Additional	preferred indications include inflammation and	inflammatory disorders.	Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliterative Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin"s disease),
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP	and regulate CREB transcription factors, and modulate expression of genes	involved in a wide variety of cell functions. Exemplary	through the cAMP response element that may be used or	routinely modified to test	activity of polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Froc Natl Acad Sci USA 85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used
*																		

				according to these assays are	melanoma, and prostate,
				publicly available (e.g.,	breast, lung, colon, pancreatic,
				through the ATCC).	esophageal, stomach, brain,
			-	Exemplary mouse T cells that	liver and urinary cancer. Other
				may be used according to these	preferred indications include
				assays include the CTLL cell	benign dysproliferative
				line, which is a suspension	disorders and pre-neoplastic
				culture of IL-2 dependent	conditions, such as, for
				cytotoxic T cells.	example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
391	HNHFU32	1339	SEAP in HIB/CRE	· ·	
392	HNHOD46	1340	SEAP in 293/ISRE		

tion		ive	nent	B		V	nent	a		An	pa	tion			hly	the	por				nent	а		(guis	cytes.	ons	ers	under
ferred the inven	ocyte	ı alternat	embodii	includes	oiting	eration.	embodii	includes	ulating	entiation	ly preferr	the inven	od for	cyte	A highly	liment of	les a met	e.g.,	ocyte	lternative	l embodii	includes	biting the	g., decrea	ing adipo	d indicati	ne disord	ed below
A highly preferred embodiment of the invention includes a method for	stimulating adipocyte	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	adipocyte proliferation.	highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation.	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under
embo	stimu	prolif	highly	of the	metho	adipo	highly	of the	metho	adipo	altern	empo	incluc	inhibi	differ	prefer	inven	for sti	increa	activa	highl	of the	metho	activa	and/o	High	inclue	(e.g.,
Kinase assay. Kinase assays, for example an Elk-1 kinase assay for FRK signal	transduction that regulate cell	proliferation or differentiation	are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature
Activation of Adipocyte ERK Signaling Pathway	Dignaming Laumay															,												
1340							***																					:
HNHOD46																												
392																												

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"Endocrine Disorders"). Highly preferred indications also include neoplastic	diseases (e.g., lipomas,	described below under	"Hyperproliferative	Disorders"). Preferred indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	winfections Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,
410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999):	the contents of each of which	reference in its entirety.	Mouse adipocyte cells that	may be used according to these assays are miblicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.								

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blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section	below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain.	highly preferred indications are complications associated with insulin resistance. Additional highly preferred	indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred	indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or

					disorders. Preferred indications include neoplasms and cancer, such as,
					lymphoma, leukemia and breast, colon, and kidney
					cancer. Additional preferred indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain, liver and urinary cancer
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
			and the second s		metaplasia, and/or dysplasia.
	HNHOD46	1340	Regulation of	Assays for the regulation of	A highly preferred indication
392			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as
				reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),

			promoter) and to regulate	diabetic neuropathy, nerve
			insulin production. The	disease and nerve damage
	•		DMEF1 response element is	(e.g., due to diabetic
			present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel
			required for insulin regulation	blockage), seizures, mental
			of Glut4 expression in skeletal	confusion, drowsiness,
			muscle. GLUT4 is the primary	nonketotic hyperglycemic-
			insulin-responsive glucose	hyperosmolar coma,
			transporter in fat and muscle	cardiovascular disease (e.g.,
-			tissue. Exemplary assays that	heart disease, atherosclerosis,
			may be used or routinely	microvascular disease,
			modified to test for DMEF1	hypertension, stroke, and other
			response element activity (in	diseases and disorders as
			adipocytes and pre-adipocytes)	described in the
			by polypeptides of the	"Cardiovascular Disorders"
			invention (including antibodies	section below), dyslipidemia,
			and agonists or antagonists of	endocrine disorders (as
			the invention) include assays	described in the "Endocrine
			disclosed inThai, M.V., et al., J	Disorders" section below),
			Biol Chem, 273(23):14285-92	neuropathy, vision impairment
		-	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
			Chem, 275(21):16323-8	blindness), ulcers and impaired
-			(2000); Liu, M.L., et al., J Biol	wound healing, and infection
			Chem, 269(45):28514-21	(e.g., infectious diseases and
			(1994); "Identification of a 30-	disorders as described in the
			base pair regulatory element	"Infectious Diseases" section
			and novel DNA binding	below, especially of the
			protein that regulates the	urinary tract and skin). An

				humon GI IITA promoter in	additional highly preferred
				transgenic mice". J Biol Chem.	indication is obesity and/or
· ·				2000 Aug 4;275(31):23666-73;	complications associated with
				Berger, et al., Gene 66:1-10	obesity. Additional highly
				(1988); and, Cullen, B., et al.,	preferred indications include
				Methods in Enzymol.	weight loss or alternatively,
		-		216:362–368 (1992), the	weight gain. Additional highly
				contents of each of which is	preferred indications are
				herein incorporated by	complications associated with
	1.49			reference in its entirety.	insulin resistance.
				Adipocytes and pre-adipocytes	
				that may be used according to	
		•		these assays are publicly	
				available (e.g., through the	
				ATCC) and/or may be	
				routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include the mouse 3T3-L1 cell	
-				line which is an adherent	
				mouse preadipocyte cell line.	
				Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3	
				fibroblasts developed through	
				clonal isolation. These cells	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				culture conditions.	
	HNHOD46	1340	Activation of	Assays for the activation of	A highly preferred indication
392			transcription	transcription inrougn ine	18 obesity and/or compileations

	through cAMP	cAMP response element are	associated with obesity.
	response element	well-known in the art and may	Additional highly preferred
	(CRE) in pre-	be used or routinely modified	indications include weight loss
_	adipocytes.	to assess the ability of	or alternatively, weight gain.
		polypeptides of the invention	An additional highly preferred
		(including antibodies and	indication is diabetes mellitus.
		agonists or antagonists of the	An additional highly preferred
		invention) to increase cAMP,	indication is a complication
		regulate CREB transcription	associated with diabetes (e.g.,
		factors, and modulate	diabetic retinopathy, diabetic
		expression of genes involved	nephropathy, kidney disease
		in a wide variety of cell	(e.g., renal failure,
		functions. For example, a	nephropathy and/or other
		3T3-L1/CRE reporter assay	diseases and disorders as
		may be used to identify factors	described in the "Renal
		that activate the cAMP	Disorders" section below),
		signaling pathway. CREB	diabetic neuropathy, nerve
		plays a major role in	disease and nerve damage
		adipogenesis, and is involved	(e.g., due to diabetic
		in differentiation into	neuropathy), blood vessel
		adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
		Exemplary assays for	confusion, drowsiness,
		transcription through the	nonketotic hyperglycemic-
		cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
		modified to test cAMP-	heart disease, atherosclerosis,
		response element activity of	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other

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diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	ce.									
diseases	describe	"Cardio	section	endocrii	describe	Disorde	neuropa	(e.g., di	blindne	wound l	(e.g., in	disorder	"Infection	below,	urinary	tunnel s	Dupuyt	Additio	indicati	associat	resistance.									
(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to
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				adipose-like conversion under	
	_			appropriate differentiation	-
				conditions known in the art.	
	HNHOD46	1340	Activation of	Assays for the activation of	A highly preferred indication
392			transcription	transcription through the	is obesity and/or complications
			through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred
			pre-adipocytes.	art and may be used or	indications include weight loss
				routinely modified to assess	or alternatively, weight gain.
				the ability of polypeptides of	An additional highly preferred
				the invention (including	indication is diabetes mellitus.
100	•			antibodies and agonists or	An additional highly preferred
				antagonists of the invention) to	indication is a complication
				regulate the serum response	associated with diabetes (e.g.,
				factors and modulate the	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in growth. Exemplary assays	(e.g., renal failure,
				for transcription through the	nephropathy and/or other
				SRE that may be used or	diseases and disorders as
				routinely modified to test SRE	described in the "Renal
				activity of the polypeptides of	Disorders" section below),
				the invention (including	diabetic neuropathy, nerve
				antibodies and agonists or	disease and nerve damage
				antagonists of the invention)	(e.g., due to diabetic
				include assays disclosed in	neuropathy), blood vessel
				Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
				(1998); Cullen and Malm,	impotence (e.g., due to diabetic
				Methods in Enzymol 216:362-	neuropathy or blood vessel
				368 (1992); Henthorn et al.,	blockage), seizures, mental
			11100	Proc Natl Acad Sci USA	confusion, drowsiness,
				85:6342-6346 (1988); and	nonketotic hyperglycemic-

				Black et al., Virus Genes	hvnerosmolar coma
				12(2):105-117 (1997), the	cardiovascular disease (e o
				content of each of which are	heart disease atherosclerosis
-		171		herein incorporated by	microvascular disease.
				reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
			***	is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
	•			continuous substrain of 3T3	(e.g., infectious diseases and
			- 4	fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
200	HNHOD46	1340	Activation of	Assays for the activation of	Preferred indications include
392			transcription	transcription through the	blood disorders (e.g., as
-4-			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described

	agonists or antagonists of the	below under "Infectious
	invention) to increase cAMP	Disease"), Preferred
	and regulate CREB	s in
	transcription factors, and	autoimmune diseases (e.g.,
	modulate expression of genes	rheumatoid arthritis, systemic
	involved in a wide variety of	lupus erythematosis, multiple
	cell functions. Exemplary	sclerosis and/or as described
	assays for transcription	below), immunodeficiencies
	through the cAMP response	(e.g., as described below),
	element that may be used or	boosting a T cell-mediated
	routinely modified to test	immune response, and
	cAMP-response element	suppressing a T cell-mediated
	activity of polypeptides of the	immune response. Additional
	invention (including antibodies	preferred indications include
	and agonists or antagonists of	inflammation and
	the invention) include assays	inflammatory disorders.
	disclosed in Berger et al., Gene	Highly preferred indications
	66:1-10 (1998); Cullen and	include neoplastic diseases
	Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
	216:362-368 (1992); Henthorn	and/or as described below
	et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Genes 15(2):105-117	indications include neoplasms
	(1997); and Belkowski et al., J	and cancers, such as, for
•	Immunol 161(2):659-665	example, leukemia, lymphoma
	(1998), the contents of each of	(e.g., T cell lymphoma,
	which are herein incorporated	Burkitt's lymphoma, non-
	by reference in its entirety. T	Hodgkins lymphoma,
	cells that may be used	Hodgkin"s disease),
	according to these assays are	melanoma, and prostate,
	publicly available (e.g.,	breast, lung, colon, pancreatic,

			•	through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, ecute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
392	HNHOD46	1340	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the

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Lastraciani motivationi	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	
the obility of notionation of	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	
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(e.g., leukemia, lymphoma, and/or as described below	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,
Exemplary mouse T cells that may be used according to these assays include the CTI L cell	line, which is an IL-2	dependent suspension culture	of I cells with cytotoxic	activity.																								
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suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced participates in IL-4 induced participates in IL-4 induced lighthy preferred embodiment of the invention and increases lighthy preferred embodiment of the invention includes a lighthy preferred embodiment of the invention includes a lighthy preferred indication is disease, plasmacytomas, and chronic myelomas, and chronic proteins produced by a large and differentiation factor proteins produced by a large variety of cells where the expression level is strongly and infertion factor level is strongly and infertion includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. A highly preferred indication is disease, plasmacytomas, and chronic proteins produced by a large and differentiation factor lession level is strongly and infertion or enhancement of mucosal immunity. Highly preferred indication is disease. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) inclu
	Production of IL-6 FMAT. IL-6 is produce by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increase IgA production (IgA plays role in mucosal immunity). IL-6 induces cytotoxic T ce Deregulated expression of I has been linked to autoimm disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulat and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines area
	HNHOD46 1340
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described below under "Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described	below) and immunodeficiencies (e.g., as described below). Highly preferred indications also	include boosting a B cell- mediated immune response and alternatively suppressing a B cell-mediated immune	response. Highly preferred indications include inflammation and inflammatory disorders. Additional highly	preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms
factors, and hormones are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function.	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and	the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely	modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "I ymphocytes: a practical

		approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using	and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and
		techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's
	18 A		lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted
			organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an

infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention	includes a method for	stimulating MIP1a production.	An alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., reducing)	MIP1a production. A highly	preferred indication is	infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below): Additional	highly preferred indications
	MIP-1alpha FMAT. Assays for immunomodulatory	proteins produced by activated	dendritic cells that upregulate	monocyte/macrophage and T	cell chemotaxis are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of
	Production of MIP1alpha					-		<u>.</u>																			
	1340													-													
	HNHOD46																										
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include inflammation and inflammatory disorders.	Preferred indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,
polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation
																												
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				and functional activities.	liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, and/or dysplasia.
392	HNHOD46	1340	SEAP in HIB/CRE		
392	HNHOD46	1340	Activation of	This reporter assay measures	Highly preferred indications
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
_				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
,				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
_				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as

described below). Preferred indications include neonlastic	diseases (e.g., lenkemia	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organe and tissues hemombilia
assays for transcription through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells
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				that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
				established from the peripheral blood of a patient with mast cell leukemia, and exhibits	
				many characteristics of immature mast cells.	
	HNHOD46	1340	Activation of	This reporter assay measures	Highly preferred indications
392			transcription through NFAT	activation of the NFA1 signaling pathway in HMC-1	include allergy, asthma, and rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
•	 110		as mast cells).	cells has been linked to	described below under
-				cytokine and chemokine	"Infectious Disease"), and
			-	production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
-				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as

		imi	immunomodulatory functions.	described below). Preferred
		Ex	Exemplary assays for	indications include neoplastic
		trai	transcription through the	diseases (e.g., leukemia,
		NF	NFAT response element that	lymphoma, melanoma,
		ma	may be used or routinely	prostate, breast, lung, colon,
	-	om	modified to test NFAT-	pancreatic, esophageal,
 		res	response element activity of	stomach, brain, liver, and
		lod	polypeptides of the invention	urinary tract cancers and/or as
	-	(inc	(including antibodies and	described below under
		agc	agonists or antagonists of the	"Hyperproliferative
		vni	invention) include assays	Disorders"). Other preferred
		dis	disclosed in Berger et al., Gene	indications include benign
		:99	66:1-10 (1998); Cullen and	dysproliferative disorders and
		Ma	Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		eta	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:	85:6342-6346 (1988); De Boer	Preferred indications include
		eta	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		eta	et al., J Immunol	leukemias, Hodgkin's disease,
		165	165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hn	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Bio	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		163	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
 		al.,	al., J Exp Med 188:527-537	granulomatous disease,
		(19	(1998), the contents of each of	inflammatory bowel disease,
		whi	which are herein incorporated	sepsis, neutropenia,
		by 1	by reference in its entirety.	neutrophilia, psoriasis,
		Ma	Mast cells that may be used	suppression of immune
		acc	according to these assays are	reactions to transplanted
		and	publicly available (e.g.,	organs and tissues, hemophilia,

hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	·
through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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	HNHOD46
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				present which signals the	
		-		presence of metabolically	
				active cells. 3T3-L1 is a	
	_			mouse preadipocyte cell line. It	
				is a continuous substrain of	
				3T3 fibroblast cells developed	
				through clonal isolation. Cells	
				were differentiated to an	
				adipose-like state before being	
				used in the screen. See Green	
				H and Meuth M., Cell 3: 127-	
				133 (1974), which is herein	
				incorporated by reference in its	
				entirety.	
	HNHOD46	1340	IL-10 in Human T-		
392			cell 2B9		
	HNHOD46	1340	SEAP in Jurkat-		
392			AP1		
9	HNHOD46	1340	Activation of	Assays for the activation of	Preferred indications include
392			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP,	Disease"). Preferred
				bind to CREB transcription	indications include
				factor, and modulate	autoimmune diseases (e.g.,
				expression of genes involved	rheumatoid arthritis, systemic

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lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),	boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include	inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred	indications include neoplasms and cancers, such as, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's	lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that	may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension
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				culture of leukemia cells that	as, for example, hyperplasia,
				produce IL-2 when stimulated.	metaplasia, and/or dysplasia.
- 48					Preferred indications include
					anemia, pancytopema,
					leukopenia, inrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
,					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HNHOD46	1340	Activation of	Assays for the activation of	Highly preferred indications
392			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),

	modulate expression of genes	immunodeficiencies (e.g., as
	involved in	described below), boosting a T
	immunomodulatory functions.	cell-mediated immune
	Exemplary assays for	response, and suppressing a T
	transcription through the	cell-mediated immune
	NFAT response element that	response. Additional highly
	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
	1498(1):1-18 (2000); De Boer	indications include neoplasms
	et al., Int J Biochem Cell Biol	and cancers, such as, for
	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. T	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,

				according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
392	HNH0D46	1340	Activation of transcription through NFKB response element in immune cells (such as basophils).	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g.,

as described below under "Immune Activity", and "Blood-Related Disorders"). Preferred indications also	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,	multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred	indications also include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described	below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for	example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary tract cancers and as described below under	"Hyperproliferative Disorders".
agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of	immunomodulatory genes. Exemplary assays for transcription through the	NFKB response element that may be used or rountinely modified to test NFKB-response element activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Basophils that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human basophil
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·	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, include neoplasmes, desophageal, stomach, brain, include neoplasmes, desophageal, stomach, brain, include neoplastic neoplasmes, brain, include neoplasmes, desophageal, stomach, brain, desophageal, stomach, desophage	nver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,
cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription	element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies
	Activation of transcription through GAS response element in immune cells (such as T-cells).	
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	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	nreferred indication is
	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4 cell line,	that may be used according to	these assays are publicly	available (e.g., through the	ATCC).										

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multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also
Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4, that may	be used according to these	assays are publicly available	(e.g., through the ATCC).				
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include anemia, pancytopenia, leukopenia, thrombocytopenia	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted	organs, asthma and allergy.	A preferred embodiment of	the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders" and/or
															Assays for the activation of	transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate serum response	factors and modulate the	expression of genes involved	in growth and upregulate the	function of prowth-related
															Activation of	transcription	through serum	response element in	immune cells (such	as natural killer	cells).								
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															HNHOD46														•
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"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.
genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.
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malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
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					is infection (e.g., an infectious
-					disease as described below
	27 GOILL				under "Infectious Disease").
0	HNHOD46	1340	Activation of	Assays for the activation of	Highly preferred indications
392			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
	_			NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

Disorders"). Highly preferred indications include neonlasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune
85:6342-6346 (1988); Valle Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NKL	cell line, which is a human	natural killer cell line	established from the peripheral	blood of a patient with large	granular lymphocytic	leukemia. This IL-2 dependent	suspension culture cell line has	a morphology resembling that	of activated NK cells.					
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					organs, asthma and allergy.
	HNHOD46	1340	Activation of	Assays for the activation of	Preferred indications
392			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
				transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
				activity of polypeptides of the	lupus erythematosis, multiple
				invention (including antibodies	sclerosis and/or as described
-				and agonists or antagonists of	below) and
				the invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
				85:6342-6346 (1988);	also include neoplastic
				Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
				272(49):30806-30811 (1997);	lymphoma, and/or as described
				Chang et al., Mol Cell Biol	below under
				18(9):4986-4993 (1998); and	"Hyperproliferative

				Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are	Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia.
				herein incorporated by reference in its entirety	lymphoma, prostate, breast,
				Human T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
en en				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
				line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
				responsive suspension-culture	Preferred indications include
				cell line.	arthritis, asthma, AIDS,
					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HNHOD46	1340	Activation of	Assays for the activation of	A highly preferred
392			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for

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stimulating T cell proliferation.	embodiment of the invention	includes a method for	inhibiting T cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	activating T cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating T cells.	A highly preferred	embodiment of the invention	includes a method for		IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,
known in the art and may be	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate IL-2	expression in T cells.	Exemplary assays for	transcription through the CD28	response element that may be	used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by
response element in	as T-cells).																												
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		reference in its entirety. T	multiple sclerosis and/or as
		cells that may be used	described below),
		according to these assays are	immunodeficiencies (e.g., as
		publicly available (e.g.,	described below), boosting a T
		through the ATCC).	cell-mediated immune
		Exemplary human T cells that	response, and suppressing a T
		may be used according to these	cell-mediated immune
		assays include the SUPT cell	response. Highly preferred
		line, which is a suspension	indications include neoplastic
		culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
		responsive T cells.	cell carcinoma, leukemia,
_			lymphoma, and/or as described
			below under
			"Hyperproliferative
			Disorders"). Highly preferred
			indications include neoplasms
		·	and cancers, such as, for
			example, melanoma (e.g.,
			metastatic melanoma), renal
•			cell carcinoma (e.g., metastatic
			renal cell carcinoma),
			leukemia, lymphoma (e.g., T
			cell lymphoma), and prostate,
			breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
	٠		liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,

A highly preferred indication includes infection (e.g.,	associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A	highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted	organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").	referred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel

disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, le.g., T cell lymphoma, non-Hodgkin's lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	
	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene
	Activation of transcription through GAS response element in immune cells (such as T-cells).	
	1340	
	HNHOD46	
	3365	

rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described	nodeficiencies bed below),	ell-mediated nse, and	suppressing a T cell-mediated	immune response. Additional preferred indications include	and	disorders.	ed indications	include blood disorders (e.g.,	elow under	"Immune Activity", "Blood-	lers", and/or	"Cardiovascular Disorders"),	e.g., viral	erculosis,	ciated with	omatosus	alignant	and/or an	infectious disease as described	Infectious	additional	ation is	idiopathic pulmonary fibrosis.	Preferred indications include	topenia,
rheumatoid arthritis, systemi lupus erythematosis, multipl sclerosis and/or as described	below), immunodeficiencies (e.g., as described below),	boosting a T cell-mediated immune response, and	suppressing a	preferred indic	inflammation and	inflammatory disorders.	Highly preferred indications	include blood	as described below under	"Immune Acti	Related Disorders", and/or	"Cardiovascul	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious dise	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic puli	Preferred indic	anemia, pancytopenia,
66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Matikainen et al., Blood 93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).														
											-														
														-											
					_																				

				leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
HNHOD46	1340 tt	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in inmunomodulatory functions.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T

transcription through the NFAT response element that may be used or routinely modified to test NFAT- response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta
1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yesen et al., J Biol Chem 268(19):14285-14293 (1993),
the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).

Hodgkin's disease, acute Iymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	>
may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
	1340
	HNHOD46
	392

		may be used or rountinely	described below). An
		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
	-	et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such
		29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
		herein incorporated by	lymphoma, and prostate,
		reference in its entirety. T	breast, lung, colon, pancreatic,
-		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,
		line, which is a suspension	metaplasia, and/or dysplasia.
		culture of IL-2 and IL-4	Preferred indications also
		responsive T cells.	include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute

		,			lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
392	HNHOD46	1340	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

	element that may be used or	lupus erythematosis, multiple
	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
-	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	pre-neoplastic conditions, such
	each of which are herein	as, for example, hyperplasia,
	incorporated by reference in its	metaplasia, and/or dysplasia.
	entirety. T cells that may be	Preferred indications include
	used according to these assays	anemia, pancytopenia,
	are publicly available (e.g.,	leukopenia, thrombocytopenia,
	through the ATCC).	Hodgkin's disease, acute
	Exemplary T cells that may be	lymphocytic anemia (ALL),
	used according to these assays	plasmacytomas, multiple
	include the SUPT cell line,	myeloma, Burkitt's lymphoma.

				of IL-2 and IL-4 responsive T cells.	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
393	HNHOG73	1341	SEAP in 293/ISRE		Disease").
393	HNHOG73	1341	Activation of transcription through cAMP response element (CRE) in preadipocytes.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of call	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease

		functions. For example a	nephropathy and/or other
	···-	177.1 1/ODE reporter occos	disposes and disputant or
	•	313-LIVONE JEPOILEI ASSAY	discases and disolucis as
		may be used to identify factors	described in the "Kenal
		that activate the cAMP	Disorders" section below),
		signaling pathway. CREB	diabetic neuropathy, nerve
		plays a major role in	disease and nerve damage
		adipogenesis, and is involved	(e.g., due to diabetic
		in differentiation into	neuropathy), blood vessel
		adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
		Exemplary assays for	confusion, drowsiness,
-		transcription through the	nonketotic hyperglycemic-
	_	cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
		modified to test cAMP-	heart disease, atherosclerosis,
		response element activity of	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
		agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
	_	Malm, Methods in Enzymol	described in the "Endocrine
		216:362-368 (1992); Henthorn	Disorders" section below),
		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
		et al., Mol Cell Biol	blindness), ulcers and impaired
		20(3):1008-1020 (2000); and	wound healing, and infection
		Klemm et al., J Biol Chem	(e.g., infectious diseases and

273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre- adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. Activation of This reporter assay measures transcription through NFKB signaling pathway in Ku812 response element in immune cells (such NFKB response element are well-known in the art and may
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to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB ("Immune Activity", and		Exemplary assays for transcription through the systemic lupus erythematosis, NFKB response element that multiple sclerosis and/or as described below) and	of	the	invention) include assays disclosed in Berger et al., Gene below under 66:1-10 (1998); Cullen and "Hyperproliferative"	l om SA	85:6342-6346 (1988); Marone et al, Int Arch Allergy melanoma, and prostate, Immunol 114(3):207-17 breast, lung, colon, pancreatic,	(1997), the contents of each of which are herein incorporated by reference in its entirety.	
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-	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis
publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1341
	HNHOG73
	393

fiboul	modified to test SRE activity	systemic lipiis erythematosis
of the	of the polypeptides of the	Crohn"s disease, multiple
invent	invention (including antibodies	sclerosis and/or as described
and ag	and agonists or antagonists of	below), immunodeficiencies
the inv	the invention) include assays	(e.g., as described below),
disclo	disclosed in Berger et al., Gene	boosting a T cell-mediated
66:1-1	66:1-10 (1998); Cullen and	immune response, and
Malm	Malm, Methods in Enzymol	suppressing a T cell-mediated
216:30	216:362-368 (1992); Henthorn	immune response. Additional
et al.,	et al., Proc Natl Acad Sci USA	highly preferred indications
85:63	85:6342-6346 (1988); Benson	include inflammation and
et al.,	et al., J Immunol 153(9):3862-	inflammatory disorders, and
3873 (3873 (1994); and Black et al.,	treating joint damage in
Virus	Virus Genes 12(2):105-117	patients with rheumatoid
(1997)	(1997), the content of each of	arthritis. An additional highly
which	which are herein incorporated	preferred indication is sepsis.
by refe	by reference in its entirety. T	Highly preferred indications
cells t	cells that may be used	include neoplastic diseases
accord	according to these assays are	(e.g., leukemia, lymphoma,
public	publicly available (e.g.,	and/or as described below
throug	through the ATCC).	under "Hyperproliferative
Exem	Exemplary T cells that may be	Disorders"). Additionally,
used a	used according to these assays	highly preferred indications
includ	include the NK-YT cell line,	include neoplasms and
which	iller	cancers, such as, for example,
cell lir	cell line with cytolytic and	leukemia, lymphoma,
cytoto	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,

					liver and urinary cancer Other
					anofossod indications in dial
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
		-,- ,-			myeloma, Burkitt's lymphoma,
		-			arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
	_				neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
***************************************					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HNHPD10	1342	Activation of	Assays for the activation of	A highly preferred indication

394	tr.	transcription	transcription through the	is obesity and/or complications
	<u> </u>	through cAMP	cAMP response element are	associated with obesity.
	re	response element	well-known in the art and may	Additional highly preferred
	<u>)</u>	(CRE) in pre-	be used or routinely modified	indications include weight loss
	ac	adipocytes.	to assess the ability of	or alternatively, weight gain.
			polypeptides of the invention	An additional highly preferred
			(including antibodies and	indication is diabetes mellitus.
			agonists or antagonists of the	An additional highly preferred
			invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other
			3T3-L1/CRE reporter assay	diseases and disorders as
			may be used to identify factors	described in the "Renal
			that activate the cAMP	Disorders" section below),
			signaling pathway. CREB	diabetic neuropathy, nerve
-			plays a major role in	disease and nerve damage
			adipogenesis, and is involved	(e.g., due to diabetic
			in differentiation into	neuropathy), blood vessel
			adipocytes. CRE contains the	blockage, heart disease, stroke,
			binding sequence for the	impotence (e.g., due to diabetic
			transcription factor CREB	neuropathy or blood vessel
			(CRE binding protein).	blockage), seizures, mental
			Exemplary assays for	confusion, drowsiness,
			transcription through the	nonketotic hyperglycemic-
-			cAMP response element that	hyperosmolar coma,
			may be used or routinely	cardiovascular disease (e.g.,
	•		modified to test cAMP-	heart disease, atherosclerosis,
			response element activity of	microvascular disease,

	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
 	 216:362-368 (1992); Henthorn	Disorders" section below),
	 et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
··	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	273:917-923 (1998), the	disorders as described in the
-	contents of each of which are	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety. Pre-	urinary tract and skin), carpal
	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
	publicly available (e.g.,	Additional highly preferred
	through the ATCC) and/or	indications are complications
	 may be routinely generated.	associated with insulin
	Exemplary mouse adipocyte	resistance.
	cells that may be used	
	 according to these assays	
 	include 3T3-L1 cells. 3T3-L1	
-W	is an adherent mouse	
	preadipocyte cell line that is a	
	continuous substrain of 3T3	
	 fibroblast cells developed	
	 through clonal isolation and	

				undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
394	HNHPD10	1342	SEAP in HIB/CRE		
	HNHPD10	1342	Activation of	This reporter assay measures	Highly preferred indications
394			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
-			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
			-	assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,

	routinaly modified to test	1 months of the control of the control
	Touring invaling to test	lymphoma, metanoma,
	GA I A3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
 	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
 	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
 	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
 -	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
	contents of each of which are	lymphoma, arthritis, AIDS,
	herein incorporated by	granulomatous disease,
	reference in its entirety. Mast	inflammatory bowel disease,
	cells that may be used	sepsis, neutropenia,
	according to these assays are	neutrophilia, psoriasis,
	publicly available (e.g.,	suppression of immune
	through the ATCC).	reactions to transplanted
	Exemplary human mast cells	organs and tissues, hemophilia,
	that may be used according to	hypercoagulation, diabetes
 	these assays include the HMC-	mellitus, endocarditis,
	1 cell line, which is an	meningitis, and Lyme Disease.

	Highly preferred indications	rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Intectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia
immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures	signaling pathway in HMC-1	human mast cell line.	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the
	Activation of transcription	through NFAT	response element in	immune cells (such	as mast cells).																			
	1342												•											
	HNHPD10															•	-							
	394												-											

	NFAT response element that	lymphoma melanoma
	to the mond on monding 1.	tymphonia, molandina,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
ar le	response element activity of	stomach, brain, liver, and
od	polypeptides of the invention	urinary tract cancers and/or as
<u></u>	(including antibodies and	described below under
38	agonists or antagonists of the	"Hyperproliferative
ui.	invention) include assays	Disorders"). Other preferred
ld.	disclosed in Berger et al., Gene	indications include benign
)9	66:1-10 (1998); Cullen and	dysproliferative disorders and
W	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
58	85:6342-6346 (1988); De Boer	Preferred indications include
et	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et	et al., J Immunol	leukemias, Hodgkin's disease,
16	165(12):7215-7223 (2000);	acute lymphocytic anemia
<u>H</u>	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
- B	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
[M	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
W	Mast cells that may be used	suppression of immune
ac	according to these assays are	reactions to transplanted
nd	publicly available (e.g.,	organs and tissues, hemophilia,
th	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
th	that may be used according to	meningitis, and Lyme Disease.

	4			these assays include the HMC-1 cell line, which is an	
				immature human mast cell line	
				estabilished from the pertpheral	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HNTBI57	1343	Activation of	This reporter assay measures	Highly preferred indications
395			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
23				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
	·			the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
		-		antagonists of the invention) to	autoimmune diseases (e.g.,
-				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred

			through the GATA3 response	indications include neonlastic
			element that may be used or	diseases (e.g., leukemia,
			routinely modified to test	lymphoma, melanoma,
			GATA3-response element	prostate, breast, lung, colon,
			activity of polypeptides of the	pancreatic, esophageal,
			invention (including antibodies	stomach, brain, liver, and
			and agonists or antagonists of	urinary tract cancers and/or as
			the invention) include assays	described below under
			disclosed in Berger et al., Gene	"Hyperproliferative
			66:1-10 (1998); Cullen and	Disorders"). Other preferred
_			Malm, Methods in Enzymol	indications include benign
			216:362-368 (1992); Henthorn	dysproliferative disorders and
			et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
			85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
			et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
			Quant Biol 64:563-571 (1999);	Preferred indications include
			Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
-			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
			contents of each of which are	lymphoma, arthritis, AIDS,
		•	herein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
-			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
	,		that may be used according to	hypercoagulation, diabetes

				these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	mellitus, endocarditis, meningitis, and Lyme Disease.
396	HNTCE26	1344	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple
				cytokines such as tumor necrosis factor alpha (TNFa),	sclerosis and/or as described below), immunodeficiencies

		_						_											~			-		<u></u>	-			
(e.g., as described below), boosting a T cell-mediated	immune response, and suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,		preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions ench as for
and the induction or inhibition of an inflammatory or	cytotoxic response. Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise brown in the art
	***											1.00.00				<u> </u>						4						
			-														-								,			

				Human dendritic cells are	example, hyperplasia,
				antigen presenting cells in	metaplasia, and/or dysplasia.
				suspension culture, which,	Preferred indications include
		·		when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
396	HNTCE26	1344	CD69 in Human T cells		
- Administration	HNTCE26	1344	Stimulation of	Assays for measuring secretion	A highly preferred
396			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication

		the ability	the ability of polyneptides of	seconiated with dishator (a &
•		the invent	the invention (including	dishetic retinonathy dishetic
			non (moranig	diabetic letinopatily, diabetic
		antioodies	antibodies and agonists or	nephropathy, kidney disease
		antagonist	antagonists of the invention) to	(e.g., renal failure,
		stimulate	stimulate insulin secretion.	nephropathy and/or other
		For examp	For example, insulin secretion	diseases and disorders as
		is measure	is measured by FMAT using	described in the "Renal
		anti-rat ins	anti-rat insulin antibodies.	Disorders" section below),
		Insulin sec	Insulin secretion from	diabetic neuropathy, nerve
		pancreatic	pancreatic beta cells is	disease and nerve damage
		upregulate	upregulated by glucose and	(e.g., due to diabetic
		also by certain	rtain	neuropathy), blood vessel
		proteins/pe	proteins/peptides, and	blockage, heart disease, stroke,
		disregulati	disregulation is a key	impotence (e.g., due to diabetic
		component	component in diabetes.	neuropathy or blood vessel
		Exemplary	Exemplary assays that may be	blockage), seizures, mental
		used or rou	used or routinely modified to	confusion, drowsiness,
		test for stir	test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (secretion (from pancreatic	hyperosmolar coma,
		cells) by p	cells) by polypeptides of the	cardiovascular disease (e.g.,
	-	invention (invention (including antibodies	heart disease, atherosclerosis,
		and agonis	and agonists or antagonists of	microvascular disease,
		the inventi	the invention) include assays	hypertension, stroke, and other
		disclosed i	disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Phys	Am J Physiol, 277(4 Pt	described in the
		2):R959-60	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	rinology,	section below), dyslipidemia,
		138(9):373	138(9):3735-40 (1997); Kim,	endocrine disorders (as
		K.H., et al.		described in the "Endocrine
		377(2):237	377(2):237-9 (1995); and,	Disorders" section below),
		Miraglia S	Miraglia S et. al., Journal of	neuropathy, vision impairment

				Biomolecular Screening	(e a dishetic retinanothy and
			•	4:193-204 (1999), the contents	blindness), ulcers and impaired
		·		of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
	110	-		pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
			~~	et al. Endocrinology 1992	
				130:167.	
0	HNTCE26	1344	Production of	Assays for measuring	Preferred embodiments of the
396			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of

Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke			A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A
agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1	expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein	incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the
			Activation of Adipocyte ERK Signaling Pathway
			1345
			HNTNC20
·			397

highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, include of e.g., e.g., lipomas, include of e.g., e.g., e.g., e.g., e.g., e.g., e.g., e.g., e.g.,	inposarcomas, and/or as described below under	"Hyperproliferative Disorders"). Preferred
hly preferred en he invention in thod for stimuls pocyte differen trative highly bodiment of the ludes a method libiting adipocy errentiation. Ferred embodin ention includes stimulating (e.grasing) adipocy vation. An alter hly preferred en he invention in thod for inhibit vation of (e.g., /or inactivating fally preferred in lude endocrine Disord docrine Disord hly preferred in lude endocrine Disord docrine Disord hly preferred in lude endocrine Disord docrine Disord hly preferred in include neoplicases (e.g., lipo include neoplicases (e.g., lipo	ribed below u	roliferativ s"). Prefe
hly pre he inve thod fo pocyte crnative bodime bodime ludes a libiting interest cential stimuls reasing vation. Any pre he inve hod fo vation for ina hly pre lude en	sarcon ribed); (S.
Silise e.e.	lps les	Hyperp Disorder
		Se .
invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which	are nerein incorporated by reference in its entirety.	Mouse adipocyte cells that may be used according to these
invention (including ant and agonists or antagon the invention) to promo inhibit cell proliferation activation, and different Exemplary assays for Exemplary of polypeptides invention (including ant and agonists or antagon the invention (including ant assays disclosed in Forral., Biol Chem 379(8-9) 1110 (1998); Le Marcha Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); and Karin, Nature 410(6824):37-40 (2001) Cobb MH, Prog Biophy Biol 71(3-4):479-500 (1 the contents of each of very home.	are nerein incorporated reference in its entirety.	adipocytused acc
inventic and ago the inve inhibit of activation Exempl kinase a used or test ERJ activity inventic and ago the inve assays of al., Biol 1110 (1 Brustel Endocri 107(2): Kyriaki Symp 6 and Kyriaki Symp 6 and	reference	Mouse a
		·

(e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. A highly preferred indication is a complication is a complication.	te is a 3 3 der tr.	te is a 3 3 der tr.	nsion,	boold,	lisease,	or as			lers",		isorders	w under	ural	ibed	ctivity	ses"),	`			cation	An	red	tion		s (e.g.,	s (e.g., abetic	s (e.g., abetic	s (e.g., abetic sease	s (e.g., abetic sease er	s (e.g., abetic sease er	s (e.g., abetic sease er	s (e.g., abetic sease er ss
te is a 3 3 4 der t. t.	te is a d d d t. t.	te is a d d d t. t.	g., hyperter	eart failure	age, heart o	tence and/c	low under	tivity",	ular Disorc	d-Related	immune d	ribed belov	tivity"), ne	3., as descr	"Neural A	gical Disea	(e.g., as	low under	isease").	ferred indiv	ellitus.	ghly prefer	a complica		ith diabete	associated with diabetes (e.g., diabetic retinopathy, diabetic	ith diabetes opathy, dia kidney dia	ith diabetes opathy, dis kidney dis illure,	ith diabetes opathy, dis kidney dis illure, and/or oth	ith diabetes opathy, dii kidney dii illure, and/or oth disorders a	ith diabetes opathy, dia kidney dis lilure, and/or oth disorders a the "Renal	ith diabetes opathy, dir kidney dis kidney dis illure, and/or othe disorders a the "Renal ction belo
(e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	(e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	disorders (e.	congestive h	vessel blocka	stroke, impo	described be	"Immune Ac	"Cardiovasco	and/or "Bloo	Disorders"),	(e.g., as desc	"Immune Ac	disorders (e.g	below under	and Neurolog	and infection	described bel	"Infectious D	A highly pred	is diabetes m	additional hig	indication is	Later Comme	associated Wi	associated wi	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease	associated wi diabetic retin nephropathy, (e.g., renal fa	associated with diabetes (diabetic retinopathy, diab nephropathy, kidney dise (e.g., renal failure, nephropathy and/or other	associated with diabetes diabetic retinopathy, diab nephropathy, kidney dise (e.g., renal failure, nephropathy and/or other diseases and disorders as	associated with diabete diabetic retinopathy, di nephropathy, kidney di (e.g., renal failure, nephropathy and/or oth diseases and disorders; described in the "Renal	associated with diabetes (e diabetic retinopathy, diabet nephropathy, kidney diseas (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
			(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																
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(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or
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dinibationa anationilamo	Compileations associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	
									-																				·		
							-							-	-																
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					liver and urinary cancer
					Highly preferred indications
					include linomas and
					include upomias and
	_				liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
 -			,		pre-neoplastic conditions, such
· .					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
397	HNTINC20	1345	TNFa in Human T-cell 2B9		
	HNTNI01	1346	Regulation of	Assays for the regulation of	A highly preferred indication
398			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as
				reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),
				promoter) and to regulate	diabetic neuropathy, nerve
				insulin production. The	disease and nerve damage
			~	DMEF1 response element is	(e.g., due to diabetic
				present in the GLUT4	neuropathy), blood vessel
				promoter and binds to MEF2	blockage, heart disease, stroke,
				transcription factor and another	impotence (e.g., due to diabetic
				transcription factor that is	neuropathy or blood vessel

ipocytes ding to ly ly ly lthe lay be e assays -L1 cell ant f 3T3 hrough c ea f 3T3 hrough c ea f 1 1 line. e a f 1 1 line. e a f 3 T3 hrough c ea f 1 1 f 1 line. e a f 3 T3 hrough c and may on of he muder ition und cention und und					contents of each of which is	preferred indications are
Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line. Whouse 3T3-L1 cell include the mouse 3T3-L1 cell include the mouse 3T3-L1 cell sare a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNIOI 1346 Activation of transcription through the through cAMP response element are response element Rough Assays for the activation of transcription through the invention (CRE) in pre- be used or routinely modified adipocytes. to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the					herein incorporated by	complications associated with
Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 9T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. Activation of transcription through the through cAMP response element cAMP response element are response element (CRE) in pre- to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the					reference in its entirety.	insulin resistance.
that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNI01 1346 Activation of Assays for the activation of transcription through the through cAMP response element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					Adipocytes and pre-adipocytes	
these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. Assays for the activation of transcription transcription transcription through the transcription (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					that may be used according to	
available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipocyte to adipocytes be used or routiniely modified agonists or antagonists of the					these assays are publicly	
ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cell line. Mouse 3T3-L1 cell sare a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNIOI 1346 Activation of Assays for the activation of transcription through the through cAMP cAMP response element are response element are response element well-known in the art and may (CRE) in pre- to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the					available (e.g., through the	
routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNI01 1346 Activation of Assays for the activation of transcription through the through cAMP exponse element are response element (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the			•		ATCC) and/or may be	
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In which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipocy-like conversion under appropriate differentiation culture conditions. Activation of Assays for the activation of transcription through the through cAMP caponse element are response element (CRE) in pre- adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					include the mouse 3T3-L1 cell	
mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNI01 1346 Activation of Assays for the activation of transcription transcription through the through cAMP response element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					line which is an adherent	
Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNI01 1346 Activation of Assays for the activation of transcription transcription through the through cAMP response element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the					mouse preadipocyte cell line.	
continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. Activation of Assays for the activation of transcription transcription through the through cAMP cAMP response element are response element well-known in the art and may (CRE) in pre- adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					Mouse 3T3-L1 cells are a	
fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HNTNI01 1346 Activation of Assays for the activation of transcription transcription through the through cAMP cAMP response element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					continuous substrain of 3T3	
HNTNI01 1346 Activation of transcription through the through cAMP response element tresponse element to adipocytes. HNTNI01 1346 Activation of transcription through the through cAMP response element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					fibroblasts developed through	
HNTNI01 1346 Activation of transcription through the through cAMP cAMP response element response element adipocytes. (CRE) in preduced adipocytes. (including antibodies and agonists of the					clonal isolation. These cells	
HNTNI01 1346 Activation of transcription through the through cAMP response element are response element are response element adipocytes. (CRE) in pre- dipocytes. adipocytes. adipocytes. adipocytes. adipocytes agonists or antagonists of the					undergo a pre-adipocyte to	
HNTNI01 1346 Activation of Assays for the activation of transcription through the transcription through the tresponse element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					adipose-like conversion under	
HNTNI01 1346 Activation of Assays for the activation of transcription transcription through the through cAMP cAMP response element are response element well-known in the art and may (CRE) in pre- be used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					appropriate differentiation	
HNTNI01 1346 Activation of transcription transcription through the through cAMP cAMP response element are response element (CRE) in pre- pe used or routinely modified adipocytes. polypeptides of the invention (including antibodies and agonists or antagonists of the					culture conditions.	
transcription transcription through the through cAMP cAMP response element are response element well-known in the art and may (CRE) in preduction to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the		HNTNI01	1346	Activation of	Assays for the activation of	A highly preferred indication
cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	398			transcription	transcription through the	is obesity and/or complications
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the				through cAMP	cAMP response element are	associated with obesity.
be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the				response element	well-known in the art and may	Additional highly preferred
to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the				(CRE) in pre-	be used or routinely modified	indications include weight loss
tion the				adipocytes.	to assess the ability of	or alternatively, weight gain.
the					polypeptides of the invention	An additional highly preferred
					(including antibodies and	indication is diabetes mellitus.
					agonists or antagonists of the	An additional highly preferred

	invention) to increase cAMP,	indication is a complication
 	regulate CREB transcription	associated with diabetes (e.g.,
	factors, and modulate	diabetic retinopathy, diabetic
	expression of genes involved	nephropathy, kidney disease
	in a wide variety of cell	(e.g., renal failure,
	functions. For example, a	nephropathy and/or other
	3T3-L1/CRE reporter assay	diseases and disorders as
	may be used to identify factors	described in the "Renal
	that activate the cAMP	Disorders" section below),
	signaling pathway. CREB	diabetic neuropathy, nerve
	plays a major role in	disease and nerve damage
	adipogenesis, and is involved	(e.g., due to diabetic
	in differentiation into	neuropathy), blood vessel
	adipocytes. CRE contains the	blockage, heart disease, stroke,
	binding sequence for the	impotence (e.g., due to diabetic
	transcription factor CREB	neuropathy or blood vessel
 	(CRE binding protein).	blockage), seizures, mental
	Exemplary assays for	confusion, drowsiness,
	transcription through the	nonketotic hyperglycemic-
	cAMP response element that	hyperosmolar coma,
	may be used or routinely	cardiovascular disease (e.g.,
 	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),

				et al., Proc Natl Acad Sci USA	neuronathy vision impairment
				85:6342-6346 (1988): Relisch	(e o dishetic retinonathy and
	_	*-		et al Mol Cell Biol	(v.g., diagone remopanty and
-		110		20(3):1008-1020 (2000): and	viound boding and infation
				20(3):1008-1020 (2000), alld Klemm et al 1 Biol Chem	Wound nearing, and infection
				773.017_073 (1008) +b.	(e.g., infectious diseases and
				2/3:71/-723 (1990), tile	"Infections Discours In the
		•		herein incorporated by	helow especially of the
				reference in its entirety. Pre-	urinary tract and skin) carnal
		7001		adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
	70.			cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
300	HNINIOI	1346	Activation of	Assays for the activation of	A highly preferred indication
398			transcription	transcription through the	is obesity and/or complications
			through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred

	pre-adipocytes.	art and may be used or	indications include weight loss
•		routinely modified to assess	or alternatively, weight gain.
	 	the ability of polypeptides of	An additional highly preferred
	 	the invention (including	indication is diabetes mellitus.
		antibodies and agonists or	An additional highly preferred
		antagonists of the invention) to	indication is a complication
		regulate the serum response	associated with diabetes (e.g.,
		factors and modulate the	diabetic retinopathy, diabetic
		expression of genes involved	nephropathy, kidney disease
		in growth. Exemplary assays	(e.g., renal failure,
		for transcription through the	nephropathy and/or other
		SRE that may be used or	diseases and disorders as
		routinely modified to test SRE	described in the "Renal
	 	activity of the polypeptides of	Disorders" section below),
		the invention (including	diabetic neuropathy, nerve
240	 -	antibodies and agonists or	disease and nerve damage
03		antagonists of the invention)	(e.g., due to diabetic
		include assays disclosed in	neuropathy), blood vessel
:		Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
		(1998); Cullen and Malm,	impotence (e.g., due to diabetic
		Methods in Enzymol 216:362-	neuropathy or blood vessel
		368 (1992); Henthorn et al.,	blockage), seizures, mental
		Proc Natl Acad Sci USA	confusion, drowsiness,
	 	85:6342-6346 (1988); and	nonketotic hyperglycemic-
		Black et al., Virus Genes	hyperosmolar coma,
		12(2):105-117 (1997), the	cardiovascular disease (e.g.,
		content of each of which are	heart disease, atherosclerosis,
		herein incorporated by	microvascular disease,
		reference in its entirety. Pre-	hypertension, stroke, and other
		adipocytes that may be used	diseases and disorders as
		according to these assays are	described in the

				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
-				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
	HNTNI01	1346	Activation of	Assays for the activation of	Highly preferred indications
398			transcription	transcription through the	include asthma, allergy,
			through GAS	Gamma Interferon Activation	hypersensitivity reactions,
			response element in	Site (GAS) response element	inflammation, and
			immune cells (such	are well-known in the art and	inflammatory disorders.
			as eosinophils).	may be used or routinely	Additional highly preferred
				modified to assess the ability	indications include immune
				of polypeptides of the	and hematopoietic disorders
				invention (including antibodies	(e.g., as described below under
				and agonists or antagonists of	"Immune Activity", and
_				the invention) to modulate	"Blood-Related Disorders"),
				gene expression (commonly	autoimmune diseases (e.g.,
				via STAT transcription factors)	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, Crohn's
				cell functions. Exemplary	disease, multiple sclerosis

and/or as described below),	immunodeficiencies (e.g., as	described below), boosting an	eosinophil-mediated immune	response and, alternatively,	suppressing an eosinophil-	mediated immune response.																								
assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed
								3=				•																		
							_																							

and/or cited in: Mayumi M., "Fol - 1 a human eocinonhilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its	entirety. Exemplary cells that	may be used according to these	assays include eosinophils.	Eosinophils are a type of	immune cell important in the	late stage of allergic reactions;	they are recruited to tissues	and mediate the inflammtory	response of late stage allergic	reaction. Increases in GAS	mediated transcription in
																			_										
																,		_										,	

r a result ormally a sokine sp. IL3,	he include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infections and indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), immunological disorders, inflammatory disorders (e.g., as described below under inflammatory disorders (e.g., as described below under "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below).	and
eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).		66:1-10 (1998); Cullen and
	transcription through NFKB response element in immune cells (such as EOL1 cells).	
	I I I I I I I I I I I I I I I I I I I	
·	398	

Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997):	Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844	which are herein incorporated by reference in its entirety.	(which measures increases in transcription inducible from a	NFKB responsive element in EOL-1 cells) may link the NFKB element to a repeorter	gene and binds to the NFKB transcription factor, which is upregulated by cytokines and	other factors. Exemplary immune cells that may be used according to these assays	include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a	type of immune cell important in the allergic responses; they	are recruited to ussues and mediate the inflammtory
				2408	· · · · · · · · · · · · · · · · · · ·				

				response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.	
	HNTNI01	1346	Regulation of	Assays for the regulation of	A highly preferred
398			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
				and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
				lipogenesisand its expression is	diabetic neuropathy, nerve
				stimulted by insulin. ME	disease and nerve damage
				promoter contains two direct	(e.g., due to diabetic
				repeat (DR1)- like elements	neuropathy), blood vessel
				MEp and MEd identified as	blockage, heart disease, stroke,
-				putative PPAR response	impotence (e.g., due to diabetic
				elements. ME promoter may	neuropathy or blood vessel
		<u>, s</u>		also responds to AP1 and other	blockage), seizures, mental
				transcription factors.	confusion, drowsiness,
	_		_	Exemplary assays that may be	nonketotic hyperglycemic-
				used or routinely modified to	hyperosmolar coma,
				test for regulation of	cardiovascular disease (e.g.,
				transcription of Malic Enzyme	heart disease, atherosclerosis,
				(in adipoocytes) by	microvascular disease,
			_	polypeptides of the invention	hypertension, stroke, and other
				(including antibodies and	diseases and disorders as

				agonists or antagonists of the	described in the
				invention) include assays	"Cardiovascular Disorders"
				disclosed in: Streeper, R.S., et	section below), dyslipidemia,
				al., Mol Endocrinol,	endocrine disorders (as
				12(11):1778-91 (1998);	described in the "Endocrine
				Garcia-Jimenez, C., et al., Mol	Disorders" section below),
				Endocrinol, 8(10):1361-9	neuropathy, vision impairment
				(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
				Biol Chem, 274(25):17997-	blindness), ulcers and impaired
				8004 (1999); Ijpenberg, A., et	wound healing, and infection
			•	al., J Biol Chem,	(e.g., infectious diseases and
				272(32):20108-20117 (1997);	disorders as described in the
	=			Berger, et al., Gene 66:1-10	"Infectious Diseases" section
				(1988); and, Cullen, B., et al.,	below, especially of the
				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
	<u></u>			according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
-				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
	_			may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HNTNI01	1346	Activation of	This reporter assay measures	Highly preferred indications
398			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred

	response element in	human mast cell line.	indications include infection
-	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the GATA3 response	Preferred indications also
		element are well-known in the	include blood disorders (e.g.,
		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
-		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
	-	disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign

				216:362-368 (1992); Henthorn	dysproliferative disorders and
				et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		-		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
0				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
_				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
		_		cell leukemia, and exhibits	
-				many characteristics of	
				immature mast cells.	
	HNTNI01	1346	Activation of	This reporter assay measures	Highly preferred indications
398			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred

	response element in	human mast cell line.	indications include infection
	immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the Nuclear Factor of	Preferred indications also
		Activated T cells (NFAT)	include blood disorders (e.g.,
		response element are well-	as described below under
		known in the art and may be	"Immune Activity", "Blood-
		used or routinely modified to	Related Disorders", and/or
		assess the ability of	"Cardiovascular Disorders").
		polypeptides of the invention	Preferred indications include
-		(including antibodies and	autoimmune diseases (e.g.,
		agonists or antagonists of the	rheumatoid arthritis, systemic
		invention) to regulate NFAT	lupus erythematosis, multiple
		transcription factors and	sclerosis and/or as described
	1000	modulate expression of genes	below) and
		involved in	immunodeficiencies (e.g., as
		immunomodulatory functions.	described below). Preferred
		Exemplary assays for	indications include neoplastic
		transcription through the	diseases (e.g., leukemia,
		NFAT response element that	lymphoma, melanoma,
		may be used or routinely	prostate, breast, lung, colon,
		modified to test NFAT-	pancreatic, esophageal,
		response element activity of	stomach, brain, liver, and
		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign

			66:1-10 (1998); Cullen and	dysproliferative disorders and
	•		Malm, Methods in Enzymol	pre-neoplastic conditions, such
			216:362-368 (1992); Henthorn	as. for example, hyperplasia.
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
			85:6342-6346 (1988); De Boer	Preferred indications include
			et al., Int J Biochem Cell Biol	anemia, pancytopenia,
			31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
			et al., J Immunol	leukemias, Hodgkin's disease,
			165(12):7215-7223 (2000);	acute lymphocytic anemia
			Hutchinson and McCloskey, J	(ALL), plasmacytomas,
			Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
			16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
			al., J Exp Med 188:527-537	granulomatous disease,
			(1998), the contents of each of	inflammatory bowel disease,
			which are herein incorporated	sepsis, neutropenia,
			by reference in its entirety.	neutrophilia, psoriasis,
		-	Mast cells that may be used	suppression of immune
			according to these assays are	reactions to transplanted
	<u> </u>		publicly available (e.g.,	organs and tissues, hemophilia,
			through the ATCC).	hypercoagulation, diabetes
			Exemplary human mast cells	mellitus, endocarditis,
			that may be used according to	meningitis, and Lyme Disease.
	.		these assays include the HMC-	
			1 cell line, which is an	
			immature human mast cell line	
			established from the peripheral	
	J-		blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HNTNI01	1346	Activation of	This reporter assay measures	Highly preferred indication

398		transcription	activation of the NFkB	includes alleray acthma and
		through NFKB	signaling nathway in HMC-1	rhinitie Additional highly
		rocnong o conont :	brungs most cell line	
			numan mast cell line.	preferred indications include
		mmnue cells (snch	Activation of NFkB in mast	infection (e.g., an infectious
		as mast cells).	cells has been linked to	disease as described below
			production of certain	under "Infectious Disease"),
			cytokines, such as IL-6 and IL-	and inflammation and
			9. Assays for the activation of	inflammatory disorders.
			transcription through the	Preferred indications include
	-		NFKB response element are	immunological and
			well-known in the art and may	hempatopoietic disorders (e.g.,
			be used or routinely modified	as described below under
-			to assess the ability of	"Immune Activity", and
			polypeptides of the invention	"Blood-Related Disorders").
			(including antibodies and	Preferred indications also
			agonists or antagonists of the	include autoimmune diseases
			invention) to regulate NFKB	(e.g., rheumatoid arthritis,
			transcription factors and	systemic lupus erythematosis,
			modulate expression of	multiple sclerosis and/or as
			immunomodulatory genes.	described below) and
-			Exemplary assays for	immunodeficiencies (e.g., as
		_	transcription through the	described below). Preferred
			NFKB response element that	indications also include
			may be used or rountinely	neoplastic diseases (e.g.,
			modified to test NFKB-	leukemia, lymphoma,
			response element activity of	melanoma, and/or as described
		. 12	polypeptides of the invention	below under
			(including antibodies and	"Hyperproliferative
			agonists or antagonists of the	Disorders"). Preferred
			invention) include assays	indications include neoplasms
			disclosed in Berger et al., Gene	and cancer, such as, for

66:1-10 (1998); Cullen and example, leukemia, lymphoma,	Malm, Methods in Enzymol melanoma, and prostate,	216:362-368 (1992); Henthorn breast, lung, colon, pancreatic,		85:6342-6346 (1988); Stassen liver, urinary tract cancers and	~			(2000),	the contents of each of which	are herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	immature human mast cell line	established from the peripheral	blood of a patient with mast	cell leukemia, and exhibits	many characteristics of	immature mast cells.	Assays for the activation of Highly preferred indications	transcription through the include allergy, asthma, and	Signal Transducers and rhinitis. Additional highly	tion	
[66:1	Mal	216	etal	85:6	etal	(200	Wal	Imm	the	are	refer	cells	acco	qnd	thro	Exel	that	these	1 ce	mmi	estal	oold	cell	man	imm	<u> </u>		through STAT6 Sign	response element in Activ	
																	-									1346				
								_																		HNTNI01				
											_						-										398		-	

as mast cells).	immune cells (such as in the	disease as described below
	human HMC-1 mast cell line)	under "Infectious Disease"),
	are well-known in the art and	and inflammation and
	may be used or routinely	inflammatory disorders.
 	modified to assess the ability	Preferred indications also
	of polypeptides of the	include hematopoietic and
	invention (including antibodies	immunological disorders (e.g.,
	and agonists or antagonists of	as described below under
	the invention) to regulate	"Immune Activity", "Blood-
	STAT6 transcription factors	Related Disorders", and/or
	and modulate the expression of	"Cardiovascular Disorders"),
	multiple genes. Exemplary	autoimmune diseases (e.g.,
	assays for transcription	rheumatoid arthritis, systemic
	through the STAT6 response	lupus erythematosis, multiple
	element that may be used or	sclerosis and/or as described
 -	routinely modified to test	below), and
 	STAT6 response element	immunodeficiencies (e.g., as
 	activity of the polypeptides of	described below). Preferred
	the invention (including	indications include neoplastic
	antibodies and agonists or	diseases (e.g., leukemia,
 	antagonists of the invention)	lymphoma, melanoma, and/or
 	include assays disclosed in	as described below under
	Berger et al., Gene 66:1-10	"Hyperproliferative
	(1998); Cullen and Malm,	Disorders"). Preferred
	Methods in Enzymol 216:362-	indications include neoplasms
	368 (1992); Henthorn et al.,	and cancer, such as, for
	Proc Natl Acad Sci USA	example, leukemia, lymphoma,
	85:6342-6346 (1988);	melanoma, and prostate,
	Sherman, Immunol Rev	breast, lung, colon, pancreatic,
	179:48-56 (2001); Malaviya	esophageal, stomach, brain,
	and Uckun, J Immunol	liver and urinary cancer. Other

				168:421-426 (2002); Masuda	preferred indications include
-				et al., J Biol Chem	benign dysproliferative
				275(38):29331-29337 (2000);	disorders and pre-neoplastic
				and Masuda et al., J Biol Chem	conditions, such as, for
				276:26107-26113 (2001), the	example, hyperplasia,
				contents of each of which are	metaplasia, and/or dysplasia.
				herein incorporated by	Preferred indications include
				reference in its entirety. Mast	hematopoietic and
				cells that may be used	immunological disorders such
				according to these assays are	as arthritis, AIDS,
		·		publicly available (e.g.,	granulomatous disease,
				through the ATCC).	inflammatory bowel disease,
				Exemplary human mast cells	sepsis, neutropenia,
				that may be used according to	neutrophilia, psoriasis,
				these assays include the HMC-	suppression of immune
				1 cell line, which is an	reactions to transplanted
				immature human mast cell line	organs and tissues, hemophilia,
				established from the peripheral	hypercoagulation, diabetes
				blood of a patient with mast	mellitus, endocarditis,
				cell leukemia, and exhibits	meningitis, and Lyme Disease.
				many characteristics of	
				immature mast cells.	
000	HNINIOI	1346	Activation of	This reporter assay measures	Highly preferred indication
398			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
			immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.

				publicly available (e.g.,	1.0000
				through the ATCC).	
				Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
				chronic myelogenous	
				leukemia. It is an immature	
				prebasophilic cell line that can	
				be induced to differentiate into	
	-			mature basophils.	
	HNTNI01	1346	SEAP in		
398			Molt4/SRE		
	HNTNI01	1346	Activation of	Assays for the activation of	Highly preferred indications
398	-		transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
	-			immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
					W

response. Additional highly preferred indications include inflammation and	inflammatory disorders. An additional highly preferred	indication is infection (e.g., an infectious disease as described	below under "Infectious	Disease"). Preferred	indications include neoplastic diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute
NFAT response element that may be used or routinely modified to test NFAT-	response element activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to
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											ato.	_	_									_	_		
																	-								

				these assays include the NK-YT cell line, which is a human	lymphocytic anemia (ALL), plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
•				activity.	disease, inflammatory bowel
′					disease, sepsis, neutropenia,
		-			neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HNTNI01	1346	SEAP in		
398			NK16/STAT6		
	HNTNI01	1346	Activation of	Assays for the activation of	Highly preferred indications
398			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
-				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
-				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,

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esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with
assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).		-		
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		_									-				.															

					chronic granulomatonic
					dironic granuoniatosas
					disease and malignant
					osteoporosis, and/or an
					infectious disease as described
					below under "Infectious
					Disease"). An additional
			-		preferred indication is
		-			idiopathic pulmonary fibrosis.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
			-		hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
0	HNTSY18	1347	Activation of	Kinase assay. Kinase assays,	A highly preferred
399			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for
			Signalling Pathway	transduction that regulate	increasing muscle cell survival
				glucose metabolism and cell	An alternative highly preferred
				survivial are well-known in the	embodiment of the invention

	art and may be used or	includes a method for
 	routinely modified to assess	decreasing muscle cell
	the chility of nothing at deep of	decident massis entre
	the ability of polypepines of	survival. A preferred
	the invention (including	embodiment of the invention
	antibodies and agonists or	includes a method for
	antagonists of the invention) to	stimulating muscle cell
	promote or inhibit glucose	proliferation. In a specific
-	metabolism and cell survival.	embodiment, skeletal muscle
	Exemplary assays for PI3	cell proliferation is stimulated.
	kinase activity that may be	An alternative highly preferred
 	used or routinely modified to	embodiment of the invention
	test PI3 kinase-induced activity	includes a method for
	of polypeptides of the	inhibiting muscle cell
	invention (including antibodies	proliferation. In a specific
	and agonists or antagonists of	embodiment, skeletal muscle
	the invention) include assays	cell proliferation is inhibited.
	disclosed in Forrer et al., Biol	A preferred embodiment of
-	Chem 379(8-9):1101-1110	the invention includes a
	(1998); Nikoulina et al.,	method for stimulating muscle
	Diabetes 49(2):263-271	cell differentiation. In a
 -	(2000); and Schreyer et al.,	specific embodiment, skeletal
	Diabetes 48(8):1662-1666	muscle cell differentiation is
	(1999), the contents of each of	stimulated. An alternative
	which are herein incorporated	highly preferred embodiment
	by reference in its entirety.	of the invention includes a
	Rat myoblast cells that may be	method for inhibiting muscle
	used according to these assays	cell differentiation. In a
	are publicly available (e.g.,	specific embodiment, skeletal
	through the ATCC).	muscle cell differentiation is
	Exemplary rat myoblast cells	inhibited. Highly preferred
	that may be used according to	indications include disorders of

the musculoskeletal system.	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus.	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other
these assays include L6 cells. I 6 is an adherent rat myoblast	cell line, isolated from primary	cultures of rat thigh muscle,	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.																							
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			diseases and disorders as
	-	-	described in the "Done"
		_	described in the neith
			Disorders" section below),
			diabetic neuropathy, nerve
			disease and nerve damage (e.g.,
-	-		due to diabetic neuropathy),
			blood vessel blockage, heart
-			disease, stroke, impotence
	_		(e.g., due to diabetic
			neuropathy or blood vessel
			blockage), seizures, mental
			confusion, drowsiness,
-		_	nonketotic hyperglycemic-
			hyperosmolar coma,
			cardiovascular disease (e.g.,
			heart disease, atherosclerosis,
			microvascular disease,
			hypertension, stroke, and other
			diseases and disorders as
			described in the
	_		"Cardiovascular Disorders"
	7.	-	section below), dyslipidemia,
			endocrine disorders (as
			described in the "Endocrine
			Disorders" section below),
			neuropathy, vision impairment
			(e.g., diabetic retinopathy and
			blindness), ulcers and impaired
			wound healing, infections
		_	(e.g., infectious diseases and
			disorders as described in the

"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additonal highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly
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neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.		A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for
		Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to
	SEAP in HIB/CRE	Activation of transcription through CD28 response element in immune cells (such as T-cells).
	1348	1348
	HOAAC90	HOAAC90
	400	400

	test CD28-response element	inhibiting the activation of
	activity of polypeptides of the	and/or inactivating T cells.
	invention (including antibodies	A highly preferred
	and agonists or antagonists of	embodiment of the invention
	the invention) include assays	includes a method for
 	disclosed in Berger et al., Gene	stimulating (e.g., increasing)
 	66:1-10 (1998); Cullen and	IL-2 production. An alternative
	Malm, Methods in Enzymol	highly preferred embodiment
	216:362-368 (1992); Henthorn	of the invention includes a
 	et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
	85:6342-6346 (1988);	reducing) IL-2 production.
	McGuire and Iacobelli, J	Additional highly preferred
	Immunol 159(3):1319-1327	indications include
	(1997); Parra et al., J Immunol	inflammation and
	166(4):2437-2443 (2001); and	inflammatory disorders.
	Butscher et al., J Biol Chem	Highly preferred indications
	3(1):552-560 (1998), the	include autoimmune diseases
	contents of each of which are	(e.g., rheumatoid arthritis,
 	herein incorporated by	systemic lupus erythematosis,
	reference in its entirety. T	multiple sclerosis and/or as
 	cells that may be used	described below),
 	according to these assays are	immunodeficiencies (e.g., as
 _	publicly available (e.g.,	described below), boosting a T
	through the ATCC).	cell-mediated immune
 -	Exemplary human T cells that	response, and suppressing a T
•	may be used according to these	cell-mediated immune
	assays include the SUPT cell	response. Highly preferred
	line, which is a suspension	indications include neoplastic
	culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
 	responsive T cells.	cell carcinoma, leukemia,
		lymphoma, and/or as described

ler	liferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	Additional highly	preferred indications include
below under	"Hyperproliferative	Disorders"	indications	and cancer	example, n	metastatic	cell carcino	renal cell c	leukemia, l	cell lymph	breast, lung	esophageal	liver and u	preferred in	benign dys	disorders a	conditions,	example, h	metaplasia	A highly p	includes in	AIDS, tube	associated	disease, an	and/or as d	under "Infe	highly pref	AIDS. A	preferred in
		-													-			-1	-										-
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					reactions to transplanted
					organs and/or tissues, uveitis,
					psoriasis, and tropical spastic
					paraparesis. Preferred
					indications include blood
					disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
1					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
				,	Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HOAAC90	1348	Activation of	Assays for the activation of	Highly preferred indications
400			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under

polypeptides of the invention	"Immune Activity". "Blood-
(including antibodies and	Related Disorders", and/or
agonists or antagonists of the	"Cardiovascular Disorders").
invention) to regulate NFKB	Highly preferred indications
transcription factors and	include autoimmune diseases
modulate expression of	(e.g., rheumatoid arthritis,
immunomodulatory genes.	systemic lupus erythematosis,
Exemplary assays for	multiple sclerosis and/or as
transcription through the	described below), and
NFKB response element that	immunodeficiencies (e.g., as
may be used or rountinely	described below). An
modified to test NFKB-	additional highly preferred
response element activity of	indication is infection (e.g.,
polypeptides of the invention	AIDS, and/or an infectious
(including antibodies and	disease as described below
agonists or antagonists of the	under "Infectious Disease").
invention) include assays	Highly preferred indications
disclosed in Berger et al., Gene	include neoplastic diseases
66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
Malm, Methods in Enzymol	lymphoma, and/or as described
 216:362-368 (1992); Henthorn	below under
 et al., Proc Natl Acad Sci USA	"Hyperproliferative
85:6342-6346 (1988); Black et	Disorders"). Highly preferred
al., Virus Gnes 15(2):105-117	indications include neoplasms
(1997); and Fraser et al.,	and cancers, such
29(3):838-844 (1999), the	as,melanoma, renal cell
contents of each of which are	carcinoma, leukemia,
herein incorporated by	lymphoma, and prostate,
reference in its entirety. T	breast, lung, colon, pancreatic,
cells that may be used	esophageal, stomach, brain,
according to these assays are	liver and urinary cancer. Other

				publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
					nemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
401	HOACB38	1349	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity).	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a

II -6 induces extotoxic T cells method for inhihiting (e o	 has been linked to autoimmune highly preferred indication is	disease, plasmacytomas, the stimulation or enhancement	myelomas, and chronic of mucosal immunity. Highly	ses.	Assays for immunomodulatory blood disorders (e.g., as	 proteins produced by a large "Immune Activity", "Blood-	variety of cells where the Related Disorders", and/or	expression level is strongly "Cardiovascular Disorders"),	regulated by cytokines, growth and infection (e.g., as	 known in the art and may be "Infectious Disease"). Highly	used or routinely modified to preferred indications include	assess the ability of autoimmune diseases (e.g.,	polypeptides of the invention rheumatoid arthritis, systemic	(including antibodies and lupus erythematosis, multiple	agonists or antagonists of the sclerosis and/or as described	invention) to mediate below) and	immunomodulation and immunodeficiencies (e.g., as	differentiation and modulate T described below). Highly	cell proliferation and function. preferred indications also	Exemplary assays that test for include boosting a B cell-	immunomodulatory proteins mediated immune response	evaluate the production of and alternatively suppressing a	cytokines, such as IL-6, and B cell-mediated immune	the stimulation and response. Highly preferred	upregulation of T cell indications include	proliferation and functional inflammation and	Continition Charles and that
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		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
-		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
-		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,
		and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's
			lymphoma, arthritis, AIDS,

	HOACB38	1349	Production of	Assays for measuring	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications
401			vCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in	include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred inflammation and inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders"

				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
				upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
				lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
				promoting immune and	
				inflammatory responses.	
	HOCNF19	1350	Activation of	Kinase assay. Kinase assays,	A highly preferred
402			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
	-		Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting

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ration.	embodin	includes	ılating	entiation.	y preferre	he invent	d for	yte	A highly	iment of	es a meth	8.6.	ocyte	ternative	embodin	includes	iting the	., decrea	ng adipoc	indicatio	e disorde	d below i	rders").	indicatio	olastic	omas,	d/or as	under	ive	ferred
adipocyte proliferation.	highly preferred embodiment	of the invention includes	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation.	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders")	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred
adipo	highly	of the	metho	adipo	alterna	empoc	includ	inhibi	differe	prefer	invent	for stil	increa	activa	highly	of the	metho	activa	and/or	Highly	includ	(e.g., 8	"Endo	Highly	also ir	diseas	liposa	descril	"Hype	Disorc
	odies	ts of	or		ation.	×	e e	d to		f the	odies	ts of		r et	1101-	-pı				သ	hang		and	Mol	99);	hich	<u> </u>		at	these
f the	ing anti	ntagonis	promote	eration,	fferentia	s for ER	at may b	modifie	induced	eptides c	ing antil	ntagonis	slude the	in Forre	:(6-8)6	Marchai	lin	stes	1999);	chem So	1999); (n)	(2001);	Siophys	-500 (19	ich of w	orated b	ntirety.	cells th	ording to
ptides o	includ	ists or a	tion) to	ll prolif	ı, and di	ry assay	tivity th	outinely	kinase-	f polype	(includ	ists or a	tion) inc	sclosed	Chem 37	98); Le	, Exp C	ol Diabe	26-132 (JM, Bio	29-48 (1, Nature):37-40	I, Prog l	-4):479	nts of ea	incorp	in its er	lipocyte	sed acco
of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these
0	. =		-	-			<u>~</u>	<u> </u>			<u>- </u>				_ _	_	Щ	—	_		<u> </u>		4		<u> </u>	<u></u>		<u> </u>	_	u
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indications include blood disorders (e.g., hypertension, congestive heart failure, blood	vessel blockage, heart disease, stroke, impotence and/or as	described below under	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve
assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte	cells that may be used according to these assays	include 3T3-L1 cells. 3T3-L1	Is an adnerent mouse preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.								-								
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disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred
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							-																		-					

indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	- 1
								-																	_					
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					esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications
					include lipomas and
					uposarcomas. Uther preferred
					dysproliferative disorders and
					pre-neoplastic conditions, such
	***************************************				as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
402	HOCNF19	1350	HLA-DR in Human T cells		
	HOCNF19	1350	Production of IL-4	IL-4 FMAT. Assays for	A highly preferred
405				immunomodulatory proteins	embodiment of the invention
				secreted by TH2 cells that	includes a method for
				stimulate B cells, T cells,	stimulating (e.g., increasing)
				macrophages and mast cells	IL-4 production. An alternative
				and promote polarization of	highly preferred embodiment
				CD4+ cells into TH2 cells are	of the invention includes a
				well known in the art and may	method for inhibiting (e.g.,
				be used or routinely modified	reducing) IL-4 production.
		<u> </u>		to assess the ability of	A highly preferred indication
				polypeptides of the invention	includes asthma. A highly
				(including antibodies and	preferred indication includes
				agonists or antagonists of the	allergy. A highly preferred
	****			invention) to mediate	indication includes rhinitis.
				immunomodulation, stimulate	Additional highly preferred
				immune cells, modulate	indications include
		·		immune cell polarization,	inflammation and
				and/or mediate humoral or	inflammatory disorders.
				cell-mediated immunity.	Highly preferred indications

Exemplary assays that test for include neoplastic diseases immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays hening disclosed in Miraglia et al., J Biomolecular Screening 4:193- "Lymphocytes: a practical approach" Chapter 6:138-160 metaplasia, and/or dysplasia. (2000); Gonzalez et al., J Clin Preferred indications include metaplasia, and/or dysplasia.	4
Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194):	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194).
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				used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	immunodeficiencies (e.g., as described below). Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred infectious disease as described below under "Infectious Disease").
403	HODDF13	1351	Regulation of transcription through the FAS promoter element in hepatocytes	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease

ļ	(including antibodies and (e.g., renal failure,	agonists or antagonists of the pephropathy and/or other	invention) to activate the FAS diseases and disorders as	promoter element in a reporter described in the "Renal	construct and to regulate Disorders' section below),	transcription of FAS, a key diabetic neuropathy, nerve	enzyme for lipogenesis. FAS disease and nerve damage	promoter is regulated by many (e.g., due to diabetic	 SREBP. Insulin increases FAS blockage, heart disease, stroke,	gene transcription in livers of impotence (e.g., due to diabetic	diabetic mice. This neuropathy or blood vessel	stimulation of transcription is blockage), seizures, mental	also somewhat glucose confusion, drowsiness,	dependent. Exemplary assays nonketotic hyperglycemic-	that may be used or routinely hyperosmolar coma,	modified to test for FAS cardiovascular disease (e.g.,	promoter element activity (in heart disease, atherosclerosis,	hepatocytes) by polypeptides microvascular disease,	of the invention (including hypertension, stroke, and other	antibodies and agonists or diseases and disorders as	antagonists of the invention) described in the	include assays disclosed in "Cardiovascular Disorders"	Xiong, S., et al., Proc Natl section below), dyslipidemia,	Acad Sci U.S.A., 97(8):3948- endocrine disorders (as	53 (2000); Roder, K., et al., described in the "Endocrine	Eur J Biochem, 260(3):743-51 Disorders" section below),	(1999); Oskouian B, et al., neuropathy, vision impairment	Biochem J, 317 (Pt 1):257-65 (e.g., diabetic retinopathy and	(1996); Berger, et al., Gene blindness), ulcers and impaired	
									 																			-		

				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
				216:362–368 (1992), the	disorders as described in the
				contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
T				according to these assays, such	Dupuytren's contracture).
				as H4IIE cells, are publicly	An additional highly preferred
				available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HODDF13	1351	Inhibition of	Reporter Assay: construct	
403			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
, <u>, , , , , , , , , , , , , , , , , , </u>				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
-				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	-
				after 72 hours. HepG2 is a	the second secon

	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection		inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include	-
human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line.	Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the	activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and aconists or	antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response
	Activation of transcription through GATA-3 response element in	immune cells (such as mast cells).		
	1351			
	HODDF13			
	403			

diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal,	urinary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including out; bodies)	and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are	herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-
	40-			
			·	

				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	,
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HODDF13	1351	Activation of	This reporter assay measures	Highly preferred indications
403			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT .	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
······································				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
	-			transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic

diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
transcription through the NFAT response element that may be used or routinely modified to test NFAT- response element activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J	Biol Chem 270(27):16333- 16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of	which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are	publicly available (e.g., through the ATCC). Exemplary human mast cells

				that may be used according to	meningius, and Lyme Disease.
				these assays include the HMC-1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
		-		many characteristics of	
				immature mast cells.	
	HODDF13	1351	Production of	Assays for measuring	Highly preferred indications
		-	VCAM in	expression of VCAM are well-	include inflammation (acute
<u> </u>			endothelial cells	known in the art and may be	and chronic), restnosis,
			such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
-				agonists or antagonists of the	inflammatory disorders,
-				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
<u>. </u>				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
<u>. </u>				tone, and immune cell	and cancers such as, for
			-	extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell

carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.		×
used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membraneassociated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.		Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Activation of Transcription
	1351	1351
	HODDF13	HODDF13
	403	403

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of
	Production of ICAM-1
	1352
	HODDN65
	404

				each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	
404	HODDN65	1352	SEAP in OE-33		
405	HODDN92	1353	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-
				variety of cells where the expression level is strongly	Related Disorders", and/or "Cardiovascular Disorders"),

and infection (e.g., as described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred
regulated by cytokines, growth factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,
			-	-						_											-								
									-					_			-	-									_	-	-
						-							-																

indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach. brain, liver and	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred
"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which,	when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

					indication is infection (e.g., an
					infectious disease as described below under "Infectious
					Disease").
	HODDN92	1353	Production of	MCP-1 FMAT. Assays for	A highly preferred
405			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for
				modified to assess the ability	inhibiting (e.g., reducing)
				of polypeptides of the	MCP-1 production. A highly
				invention (including antibodies	preferred indication is
				and agonists or antagonists of	infection (e.g., an infectious
				the invention) to mediate	disease as described below
				immunomodulation, induce	under "Infectious Disease").
				chemotaxis, and modulate	Additional highly preferred
				immune cell activation.	indications include
				Exemplary assays that test for	inflammation and
				immunomodulatory proteins	inflammatory disorders.
				evaluate the production of cell	Preferred indications include
				surface markers, such as	blood disorders (e.g., as
				monocyte chemoattractant	described below under
				protein (MCP), and the	"Immune Activity", "Blood-
				activation of monocytes and T	Related Disorders", and/or
				cells. Such assays that may be	"Cardiovascular Disorders").
				used or routinely modified to	Highly preferred indications
				test immunomodulatory and	include autoimmune diseases
				diffferentiation activity of	(e.g., rheumatoid arthritis,

	polypeptides of the invention	systemic lupus erythematosis,
	(including antibodies and	multiple sclerosis and/or as
,	agonists or antagonists of the	described below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Miraglia et al., J	described below). Preferred
	Biomolecular Screening 4:193-	indications also include
 	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160	Hodgkin's disease, acute
	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the	disease, inflammatory bowel
	contents of each of which are	disease, sepsis, neutropenia,
	herein incorporated by	neutrophilia, psoriasis,
	reference in its entirety.	suppression of immune
	Human dendritic cells that may	reactions to transplanted
	be used according to these	organs and tissues,
	assays may be isolated using	hemophilia, hypercoagulation,
	techniques disclosed herein or	diabetes mellitus, endocarditis,
	otherwise known in the art.	meningitis (bacterial and
	Human dendritic cells are	viral), Lyme Disease, asthma,
	antigen presenting cells in	and allergy Preferred
	suspension culture, which,	indications also include
	when activated by antigen	neoplastic diseases (e.g.,
	and/or cytokines, initiate and	leukemia, lymphoma, and/or as
 	upregulate T cell proliferation	described below under
	and functional activities.	"Hyperproliferative
		Disorders"). Highly preferred
		indications include neoplasms

					and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer. Other
					preferred indications include
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
	TICHONO	1253	D. 1	MIN 1-1-1- ENGATE A	metaptasia, and/or dyspiasia.
405	HODDIN92	1333	Froduction of	MIF-Taipha FMA I. Assays	A highly preferred
)			ואזון ומולווומ	aroteine produced by activated	includes a method for
				dendaria produced by activated	stimulating MID19 moduation
				monocate/mocrophene and T	An alternative bights moferned
				monocyte/macrophage and r	An ancimant of the invention
				known in the art and may he	includes a method for
				used or routinely modified to	inhibiting (e.g., reducing)
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	ıis
				(including antibodies and	infection (e.g., an infectious
				agonists or antagonists of the	disease as described below
				invention) to mediate	under "Infectious Disease").
				immunomodulation, modulate	Preferred indications include
				chemotaxis, and modulate T	blood disorders (e.g., as
				cell differentiation. Exemplary	described below under
				assays that test for	"Immune Activity", "Blood-
				immunomodulatory proteins	Related Disorders", and/or
				evaluate the production of	"Cardiovascular Disorders").
				chemokines, such as	Highly preferred indications

			macrophage inflammatory	include autoimmune diseases
 			protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
 			the activation of	systemic lupus erythematosis,
			monocytes/macrophages and T	multiple sclerosis and/or as
			cells. Such assays that may be	described below) and
			used or routinely modified to	immunodeficiencies (e.g., as
			test immunomodulatory and	described below). Additional
			chemotaxis activity of	highly preferred indications
	-		polypeptides of the invention	include inflammation and
			(including antibodies and	inflammatory disorders.
		•	agonists or antagonists of the	Preferred indications also
			invention) include assays	include anemia, pancytopenia,
			disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
 	,		Biomolecular Screening 4:193-	Hodgkin's disease, acute
 			204(1999); Rowland et al.,	lymphocytic anemia (ALL),
 			"Lymphocytes: a practical	plasmacytomas, multiple
			approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
			(2000); Satthaporn and	arthritis, AIDS, granulomatous
			Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
	-		45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
 			al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
 			29 (2000); Verhasselt et al., J	suppression of immune
			Immunol 158:2919-2925	reactions to transplanted
			(1997); and Nardelli et al., J	organs and tissues, hemophilia,
			Leukoc Biol 65:822-828	hypercoagulation, diabetes
 			(1999), the contents of each of	mellitus, endocarditis,
 			which are herein incorporated	meningitis, Lyme Disease,
-			by reference in its entirety.	asthma, and allergy.
	- ,		Human dendritic cells that may	Preferred indications also
			be used according to these	include neoplastic diseases
			assays may be isolated using	(e.g., leukemia, lymphoma,

				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
-				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
-					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HODDN92	1353	Regulation of	Assays for the regulation of	A highly preferred
405			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
		,	promoter element	known in the art and may be	indication is a complication
			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve
				enzyme for lipogenesis. FAS	disease and nerve damage
				promoter is regulated by many	(e.g., due to diabetic
				transcription factors including	neuropathy), blood vessel

		SREBP. Insulin increases FAS	blockage, heart disease, stroke.
-	0.1		impotence (e.g., due to diabetic
		diabetic mice. This	neuropathy or blood vessel
	S	stimulation of transcription is	blockage), seizures, mental
	8	also somewhat glucose	confusion, drowsiness,
	9	dependent. Exemplary assays	nonketotic hyperglycemic-
		that may be used or routinely	hyperosmolar coma,
		modified to test for FAS	cardiovascular disease (e.g.,
		promoter element activity (in	heart disease, atherosclerosis,
	4	hepatocytes) by polypeptides	microvascular disease,
	0	of the invention (including	hypertension, stroke, and other
	8	antibodies and agonists or	diseases and disorders as
	8	antagonists of the invention)	described in the
		include assays disclosed in	"Cardiovascular Disorders"
		Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	7	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	2	53 (2000); Roder, K., et al.,	described in the "Endocrine
	<u> </u>	Eur J Biochem, 260(3):743-51	Disorders" section below),
		(1999); Oskouian B, et al.,	neuropathy, vision impairment
	<u> </u>	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
		(1996); Berger, et al., Gene	blindness), ulcers and impaired
	9	56:1-10 (1988); and, Cullen,	wound healing, and infection
	<u> </u>	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
		216:362–368 (1992), the	disorders as described in the
		contents of each of which is	"Infectious Diseases" section
	4	herein incorporated by	below, especially of the
		reference in its entirety.	urinary tract and skin), carpal
	1	Hepatocytes that may be used	tunnel syndrome and
	<u> </u>	according to these assays, such	Dupuytren's contracture).
	<u>a</u>	as H4IIE cells, are publicly	An additional highly preferred
	aa	available (e.g., through the	indication is obesity and/or

				ATCC) and/or may be	complications associated with
	,.			routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
!	HODDN92	1353	Activation of	This reporter assay measures	Highly preferred indications
405			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	-		as mast cells).	cells has been linked to	described below under
<u>.</u>				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred

indications include neoplastic	lymphoma melanoma	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes
through the GATA3 response	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to
				-									-				•						_		•				

Exemplary assays for transcription through the MFAT response element that may be used or routinely modified to test NFAT-response element activity of pancreatic, esophageal, response element activity of pancreatic, esophageal, response element activity of polypeptides of the invention polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays (including antibodies and agonists or antagonists of the invention) include assays (including antibodies and Agonists or antagonists of the invention) include assays (including antibodies and Malm, Methods in Enzymol disclosed in Berger et al., Gene (1998); Cullen and Malm, Methods in Enzymol as, for example, hyperplasia. 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol anemia, pancytopenia, et al., Immunol at al.,		
Exemplary assays transcription through NFAT response element a may be used or rou modified to test NH response element a polypeptides of the (including antibodi agonists or antagor invention) include disclosed in Berger 66:1-10 (1998); Cu Malm, Methods in 216:362-368 (1992 et al., Proc Natl Ac 85:6342-6346 (198 et al., Int J Biocher 31(10):1221-1236 et al., J Immunol 165(12):7215-7223 Hutchinson and Mc Biol Chem 270(27) 16338 (1998), the content which are herein in by reference in its e Mast cells that may according to these e	Exemplary assays transcription throu, NFAT response element a modified to test NF response element a polypeptides of the (including antibodi agonists or antagor invention) include disclosed in Bergei 66:1-10 (1998); Cu Malm, Methods in 216:362-368 (1992 et al., Proc Natl Ac 85:6342-6346 (198 et al., Int J Biocher 31(10):1221-1236 et al., I munuol 165(12):7215-7223 Hutchinson and Mc Biol Chem 270(27) 16338 (1995), and al., J Exp Med 188 (1998), the content which are herein in by reference in its e Mast cells that may according to these	Exemplary assays for transcription through the NFAT response element may be used or routinel modified to test NFAT response element activity polypeptides of the inve (including antibodies ar agonists or antagonists invention) include assay disclosed in Berger et al. (including modified in Enzy 216:362-368 (1998); Cullen Malm, Methods in Enzy 216:362-368 (1998); Cullen 16:362-368 (1998); Let al., Int J Biochem Cei 31(10):1221-1236 (1998) et al., J Immunol 165(12):7215-7223 (200 Hutchinson and McClos Biol Chem 270(27):163 (1998), the contents of which are herein incorp by reference in its entire Mast cells that may be a according to these assay

				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to these assays include the HMC-	meningitis, and Lyme Disease.
				1 cell line, which is an	
				immature human mast cell line	
·				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HODDN92	1353	Activation of	Kinase assay. JNK and p38	A highly preferred
405			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
,				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention
				antagonists of the invention) to	includes a method for
				promote or inhibit cell	stimulating endothelial cell
				proliferation, activation, and	proliferation. An alternative
				apoptosis. Exemplary assays	highly preferred embodiment
				for JNK and p38 kinase	of the invention includes a
			-	activity that may be used or	method for inhibiting
				routinely modified to test JNK	endothelial cell proliferation.
				and p38 kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
				invention (including antibodies	includes a method for
				and agonists or antagonists of	stimulating apoptosis of

												_	_																
endothelial cells. An	anternative nigniy preferred	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a
the invention) include the	assays disclosed in Forrer et	ai., 5101 Chell 3/3(8-3):1101- 1110 (1998): Gunta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	
												,																	

method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of	the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications	include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins

and/or lymphatics). Highly preferred are indications that	sumulate angiogenesis and/or cardiovascularization. Highly preferred are indications that	inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors, leukemias and Kanosi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign
													-			-	-			•					
										4.								-							

dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis.	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis: venous and	lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer Highly	preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis,
			, , , , , , , , , , , , , , , , , , ,

}					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HODDO08	1354	Activation of	Assays for the activation of	A highly preferred
			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for
			response element in	known in the art and may be	stimulating T cell proliferation.
			immune cells (such	used or routinely modified to	An alternative highly preferred
			as T-cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for
				(including antibodies and	inhibiting T cell proliferation.
				agonists or antagonists of the	A highly preferred
				invention) to stimulate IL-2	embodiment of the invention
				expression in T cells.	includes a method for
				Exemplary assays for	activating T cells. An
				transcription through the CD28	alternative highly preferred
				response element that may be	embodiment of the invention
				used or routinely modified to	includes a method for
				test CD28-response element	inhibiting the activation of
				activity of polypeptides of the	and/or inactivating T cells.
				invention (including antibodies	A highly preferred
				and agonists or antagonists of	embodiment of the invention
				the invention) include assays	includes a method for
				disclosed in Berger et al., Gene	stimulating (e.g., increasing)
				66:1-10 (1998); Cullen and	IL-2 production. An alternative

Malm, Methods in Enzymol 216:362-368 (1998); 85:634-6346 (1988); McGuire and Jacobelli, J Immunol 159(3):1319-1312 Indication includes a method for inhibiting (e.g., Reducing, IL-2 production. Additional highly preferred inflammation and 166(4):2437-2443 (2001); and 166(4):2438-2443 (2001); and 166(4):243
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and lacobelli, J Immunol 195(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Immunol 160(4):2437-2443 (2001); and Butscher et al., J Immunol 161:52-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.

leukemia, Jymphoma (e.g., T cell Jymphoma), and prostate, breast, lung, colon, panereatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dsproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). Alighly preferred indication is clude suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic panaparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		cell carcinoma (e.g., metastatic renal cell carcinoma),
cell lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and unitary cancer. Other preferred indications include benign dysproliferative disorders and pre-reoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections disease, and osteoporosis, and/or as described below under "Infectious Disease,"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include bloow disorders (e.g., as described below under "Immune below under "Immune		leukemia, lymphoma (e.g., T
esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia. A highly preferred indication includes infection (e.g., AIDS, ubercolosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune	 	cell lymphoma), and prostate, breast, lung, colon, pancreatic,
liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indication is cated suppression of immune reactions to transplanted organs and/or itssues, uveitis, psoriasis, and topical spastic paraparesis. Preferred indications include suppression of immune reactions to transplanted organs and/or itssues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		esophageal, stomach, brain,
preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune The properties of the properties of the parapares of the properties of the parapares of the properties of		liver and urinary cancer. Other
benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberoulosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs andor tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		preferred indications include
disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		benign dysproliferative
conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		disorders and pre-neoplastic
example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indication is organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune paraparesis.").		conditions, such as, for
metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune	 	example, hyperplasia,
A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune "Immune "Immune" "Immune "Imm		metaplasia, and/or dysplasia.
includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune	 <u> </u>	A highly preferred indication
AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune	 	includes infection (e.g.,
associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune")		AIDS, tuberculosis, infections
disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune	 	associated with granulomatous
and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		disease, and osteoporosis,
under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		and/or as described below
highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		under "Infectious Disease"). A
AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		highly preferred indication is
preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		AIDS. Additional highly
suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		preferred indications include
reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		suppression of immune
organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune")		reactions to transplanted
psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		organs and/or tissues, uveitis,
paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune		psoriasis, and tropical spastic
indications include blood disorders (e.g., as described below under "Immune")		paraparesis. Preferred
disorders (e.g., as described below under "Immune")		indications include blood
below under "Immune		disorders (e.g., as described
		below under "Immune

Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").	include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	plasmacytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel	disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes	mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating MIP 1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP 1a production. A highly preferred indication is infection (e.g., an infectious disease as described below.	under "Infectious Disease").
					MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) to mediate
					Production of MIP1alpha	
					1355	
					HODDW40	
					407	

_	immi	imminomodulation modulate	Drafarrad indications include
	meric	ontovic and modulate T	blood disorders (e.g. es
		u r.c	blood disorders (e.g., as
	cell d	cell differentiation. Exemplary	described below under
	assay	assays that test for	"Immune Activity", "Blood-
	ımmı	immunomodulatory proteins	Related Disorders", and/or
	evalu	evaluate the production of	"Cardiovascular Disorders").
-	chem	chemokines, such as	Highly preferred indications
	macr	macrophage inflammatory	include autoimmune diseases
	prote	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the ac	the activation of	systemic lupus erythematosis,
	monc	monocytes/macrophages and T	multiple sclerosis and/or as
	cells.	cells. Such assays that may be	described below) and
•	pesn	used or routinely modified to	immunodeficiencies (e.g., as
	test ii	test immunomodulatory and	described below). Additional
	chem	chemotaxis activity of	highly preferred indications
	polyr	polypeptides of the invention	include inflammation and
	(inch	(including antibodies and	inflammatory disorders.
	agon	agonists or antagonists of the	Preferred indications also
	inver	invention) include assays.	include anemia, pancytopenia,
	discle	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
	Biom	Biomolecular Screening 4:193-	Hodgkin's disease, acute
	204()	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	"Lyn	"Lymphocytes: a practical	plasmacytomas, multiple
	appro	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
	(2000	(2000); Satthaporn and	arthritis, AIDS, granulomatous
	Erem	Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
	45(1)	45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
	al., T	al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
	29 (2	29 (2000); Verhasselt et al., J	suppression of immune
	Imm	Immunol 158:2919-2925	reactions to transplanted
	(1997)	(1997); and Nardelli et al., J	organs and tissues, hemophilia,

4	incrapiasia, and/or dyspiasia.		lys for Preferred embodiments of the invention include using
Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	u	ii.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be
J	Glucose Production in H4IIE	SEAP in HepG2/Squale- synthetase(stimulati	Regulation of apoptosis of immune cells (such
	1355	1355	1355
	HODDW40	HODDW40	HODDW40
·	407	407	407

(or antibodies, agonists, or	antagonists thereof) in	detection, diagnosis,	prevention, and/or treatment of	asthma, allergy,	hypersensitivity and	inflammation.																								
used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate caspase	protease-mediated apoptosis in	immune cells (such as, for	example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);
as mast cells).																														
						-							74.5																-	

		A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred
Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.		Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of
	SEAP in OE-33	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway
	1355	1356
	HODDW40	HODEJ32
	407	408

	the invention (including	embodiment of the invention
	distriction and against or	includes a method for
-	alithodics and agoinsts of	
	antagonists of the invention) to	stimulating muscle cell
-	promote or inhibit glucose	proliferation. In a specific
	metabolism and cell survival.	embodiment, skeletal muscle
	Exemplary assays for PI3	cell proliferation is stimulated.
	kinase activity that may be	An alternative highly preferred
	used or routinely modified to	embodiment of the invention
3	test PI3 kinase-induced activity	includes a method for
	of polypeptides of the	inhibiting muscle cell
	invention (including antibodies	proliferation. In a specific
	and agonists or antagonists of	embodiment, skeletal muscle
	the invention) include assays	cell proliferation is inhibited.
	disclosed in Forrer et al., Biol	A preferred embodiment of
	Chem 379(8-9):1101-1110	the invention includes a
	(1998); Nikoulina et al.,	method for stimulating muscle
	Diabetes 49(2):263-271	cell differentiation. In a
	(2000); and Schreyer et al.,	specific embodiment, skeletal
	Diabetes 48(8):1662-1666	muscle cell differentiation is
	(1999), the contents of each of	stimulated. An alternative
	which are herein incorporated	highly preferred embodiment
	by reference in its entirety.	of the invention includes a
	Rat myoblast cells that may be	method for inhibiting muscle
	used according to these assays	cell differentiation. In a
	are publicly available (e.g.,	specific embodiment, skeletal
	through the ATCC).	muscle cell differentiation is
	Exemplary rat myoblast cells	inhibited. Highly preferred
	that may be used according to	indications include disorders of
	these assays include L6 cells.	the musculoskeletal system.
	L6 is an adherent rat myoblast	Preferred indications include
	cell line, isolated from primary	neoplastic diseases (e.g., as
	cell line, isolated from primary	neopiasuc c

																											-		
described below under "Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),
cultures of rat thigh muscle, that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.																										
									ner sår									-10					- 14 						
										-	-																		-
				-																			-						

			diabetic neuropathy, nerve
			disease and nerve damage (e.g.,
			due to diabetic neuropathy),
			blood vessel blockage, heart
		-	disease, stroke, impotence
-			(e.g., due to diabetic
			neuropathy or blood vessel
			blockage), seizures, mental
			confusion, drowsiness,
-			nonketotic hyperglycemic-
			hyperosmolar coma,
			cardiovascular disease (e.g.,
			heart disease, atherosclerosis,
			microvascular disease,
			hypertension, stroke, and other
-			diseases and disorders as
-			described in the
			"Cardiovascular Disorders"
	-		section below), dyslipidemia,
			endocrine disorders (as
			described in the "Endocrine
			Disorders" section below),
			neuropathy, vision impairment
			(e.g., diabetic retinopathy and
			blindness), ulcers and impaired
			wound healing, infections
			(e.g., infectious diseases and
			disorders as described in the
			"Infectious Diseases" section
			below, especially of the
			urinary tract and skin), carpal

tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively.	weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additional highly preferred indications are disorders of the musculoskeletal system	muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy,	atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities,	heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach,

esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein insorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
	1357
	HODFN71
	409

					entirety.	
HODFN71 1357 Activation of transcription through the transcription trough serum Serum Response Element response element in (SRE) are well-known in the immune cells (such art and may be used or as T-cells). Toutinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthon 216:362-368 (1992); Henthon	409	HODFN71	1357	IL-2 in Human T-cell 293T		·
transcription transcription through the through serum response element in (SRE) are well-known in the immune cells (such art and may be used or a st T-cells). The ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malin, Methods in Enzymol		HODFN71	1357	Activation of	Assays for the activation of	A preferred embodiment of
through serum response element in immune cells (such immune cells (such immune cells). as T-cells). the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	409			transcription	transcription through the	the invention includes a
(SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol				through serum	Serum Response Element	method for inhibiting (e.g.,
art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn				response element in	(SRE) are well-known in the	reducing) TNF alpha
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn				immune cells (such	art and may be used or	production. An alternative
or ion) to ion) to e e the ed et che ed s. s. inholy tivity ne ibodies ists of ssays l., Gene and mol				as T-cells).	routinely modified to assess	highly preferred embodiment
or tion) to e e the e the ed s. s. s. innely tivity tivity tivity tists of ists of ists of ssays l., Gene and mol					the ability of polypeptides of	of the invention includes a
					the invention (including	method for stimulating (e.g.,
					antibodies and agonists or	increasing) TNF alpha
					antagonists of the invention) to	production. Preferred
n he fee					regulate serum response	indications include blood
n e t s					factors and modulate the	disorders (e.g., as described
in the state of th					expression of genes involved	below under "Immune
8 9 c					in growth and upregulate the	Activity", "Blood-Related
8 9 0					function of growth-related	Disorders", and/or
8 9 c					genes in many cell types.	"Cardiovascular Disorders"),
8 2 5					Exemplary assays for	Highly preferred indications
s e					transcription through the SRE	include autoimmune diseases
					that may be used or routinely	(e.g., rheumatoid arthritis,
					modified to test SRE activity	systemic lupus erythematosis,
					of the polypeptides of the	Crohn"s disease, multiple
			-		invention (including antibodies	sclerosis and/or as described
9 5					and agonists or antagonists of	below), immunodeficiencies
rene 1					the invention) include assays	(e.g., as described below),
l om					disclosed in Berger et al., Gene	boosting a T cell-mediated
E					66:1-10 (1998); Cullen and	immune response, and
					Malm, Methods in Enzymol	suppressing a T cell-mediated
┪					216:362-368 (1992); Henthorn	immune response. Additional

et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	et al., Proc Natl Acad Sci 85:6342-6346 (1988); Bel et al., J Immunol 153(9);3 3873 (1994); and Black et Virus Genes 12(2):105-11 (1997), the content of eac which are herein incorpor by reference in its entirety. Human T cells that may be used according to these as are publicly available (e.g. through the ATCC). Exemplary human T cells may be used according to assays include the JURK/cell line, which is a suspeculture of leukemia cells through the ATCC.	USA highly preferred indications include inflammation and				h of arthritis. An additional highly	ated preferred indication is sepsis.	'. Highly preferred indications	e include neoplastic diseases	says (e.g., leukemia, lymphoma,		under "Hyperproliferative	that Disorders"). Additionally,	these highly preferred indications	AT include neoplasms and	nsion cancers, such as, leukemia,	_	lated. (e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	Jenkonenia thrombocytonenia
		et al., Proc Natl Acad Sci USA 85.6342-6346 (1988). Benson	et al., J Immunol 153(9):3	3873 (1994); and Black et al.,	Virus Genes 12(2):105-11	(1997), the content of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these as	are publicly available (e.g	through the ATCC).	Exemplary human T cells	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that	produce IL-2 when stimulated.				-									

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		ugh the include blood disorders (e.g., f Activated T as described below under ponse element "Immune Activity", "Bloodnithe art and Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases
	in SRE	Activation of Assays for the activation of transcription through the through NFAT Nuclear Factor of Activated T response element in munue cells (Such are well-known in the art and as natural killer may be used or routinely modified to assess the ability of polypeptides of the invantion (including artibodies)
	SEAP in Molt4/SRE	1357 Activations transc through the second
	HODFN71	HODFN71
	409	409

and agonists or antagonists of	systemic lupus erythematosis.
the invention) to regulate	multiple sclerosis and/or as
NFAT transcription factors and	
modulate expression of genes	immunodeficiencies (e.g., as
involved in	described below), boosting a T
immunomodulatory functions.	cell-mediated immune
 Exemplary assays for	response, and suppressing a T
transcription through the	cell-mediated immune
NFAT response element that	response. Additional highly
may be used or routinely	preferred indications include
modified to test NFAT-	inflammation and
response element activity of	inflammatory disorders. An
polypeptides of the invention	additional highly preferred
(including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
invention) include assays	below under "Infectious
disclosed in Berger et al., Gene	b Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
216:362-368 (1992); Henthorn	
 et al., Proc Natl Acad Sci USA	below under
85:6342-6346 (1988);	"Hyperproliferative
Aramburu et al., J Exp Med	Disorders"). Preferred
182(3):801-810 (1995); De	indications include neoplasms
 Boer et al., Int J Biochem Cell	and cancers, such as, for
Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign

			are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC).	dysproliterative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia,
			Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sensis, neutropenia
-				neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HODFN71	1357	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g.,

	,			antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
	-	•		factors and modulate the	disorders (e.g., as described
		-		expression of genes involved	below under "Immune
			<u></u>	in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
		*		genes in many cell types.	"Cardiovascular Disorders"),
			_	Exemplary assays for	Highly preferred indications
_				transcription through the SRE	include autoimmune diseases
		•		that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
	***			of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
		-		66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
				216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications
				85:6342-6346 (1988); Benson	include inflammation and
				et al., J Immunol 153(9):3862-	inflammatory disorders, and
				3873 (1994); and Black et al.,	treating joint damage in
				Virus Genes 12(2):105-117	patients with rheumatoid
				(1997), the content of each of	arthritis. An additional highly
				which are herein incorporated	preferred indication is sepsis.
	•			by reference in its entirety. T	Highly preferred indications
				cells that may be used	include neoplastic diseases
				according to these assays are	(e.g., leukemia, lymphoma,
				publicly available (e.g.,	and/or as described below
				through the ATCC).	under "Hyperproliferative

be Disorders"). Additionally,	ays highly preferred indications	e, include neoplasms and	iller cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues hemonhilia
Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.																								_	
		-																												
										-																				

hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for includes a method for includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention embodiment of the invention	includes a method for
		Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays
	SEAP in NK16/STAT6	Activation of transcription through CD28 response element in immune cells (such as T-cells).	
	1357	1357	
	HODFN71	HODFN71	
	409	409	

stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g.	reducing) IL-2 production. Additional highly preferred indications include	inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis.	systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as	described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune	indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia,	lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci 11SA method for inhibiting (e.g., increasing) increasing)	85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327	166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are	herein incorporated by reference in its entirety. T cells that may be used according to these assays are	publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these according to these	line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	

				disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
HODFN71	1357	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
			invention) to regulate INFKB transcription factors and	rigniy preierred indications include autoimmune diseases

				line, which is a suspension	metaplasia, and/or dysplasia.
				culture of IL-2 and IL-4	Preferred indications also
				responsive T cells.	include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HODGE68	1358	Activation of	Assays for the activation of	A preferred embodiment of
410			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
·			as T-cells).	routinely modified to assess	highly preferred embodiment
				the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described

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		expression of genes involved	pelow under immune
		in growth and upregulate the	Activity", "Blood-Related
		function of growth-related	Disorders", and/or
		genes in many cell types.	"Cardiovascular Disorders"),
		Exemplary assays for	Highly preferred indications
		transcription through the SRE	include autoimmune diseases
		that may be used or routinely	(e.g., rheumatoid arthritis,
		modified to test SRE activity	systemic lupus erythematosis,
	•	of the polypeptides of the	Crohn"s disease, multiple
		invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below), immunodeficiencies
		the invention) include assays	(e.g., as described below),
		disclosed in Berger et al., Gene	boosting a T cell-mediated
		66:1-10 (1998); Cullen and	immune response, and
		Malm, Methods in Enzymol	suppressing a T cell-mediated
		216:362-368 (1992); Henthorn	immune response. Additional
		et al., Proc Natl Acad Sci USA	highly preferred indications
		85:6342-6346 (1988); Benson	include inflammation and
		et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety.	Highly preferred indications
		Human T cells that may be	include neoplastic diseases
		used according to these assays	(e.g., leukemia, lymphoma,
 		are publicly available (e.g.,	and/or as described below
		through the ATCC).	under "Hyperproliferative
		Exemplary human T cells that	Disorders"). Additionally,
 		may be used according to these	highly preferred indications
		assays include the JURKAT	include neoplasms and